UNITED NATIONS

UNEP

Food and Agriculture Organization of the United Nations

RC

UNEP/FAO/RC/CRC.14/1

Distr.: General
15 May 2018

English only

Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade

Chemical Review Committee
Fourteenth meeting
Rome, 11–14 September 2018

Provisional agenda

1. Opening of the meeting.
2. Organizational matters:
   - (a) Adoption of the agenda;
   - (b) Organization of work.
3. Rotation of the membership.
4. Technical work:
   - (a) Consideration of draft decision guidance documents:
     - (i) Acetochlor;
     - (ii) Hexabromocyclododecane;
     - (iii) Phorate.
   - (b) Report of the Bureau on the preliminary review of notifications of final regulatory action;
   - (c) Review of notifications of final regulatory action:
     - (i) Hexabromocyclododecane;
     - (ii) Methyl parathion;
     - (iii) Perfluorooctanoic acid (PFOA), its salts and PFOA-related compounds.
5. Updates to the Handbook of Working Procedures and Policy Guidance for the Chemical Review Committee.
6. Venue and date of the fifteenth meeting of the Committee.
7. Other matters.
8. Adoption of the report.
9. Closure of the meeting.

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UNITED NATIONS

UNEP

Food and Agriculture Organization of the United Nations

RC

UNEP/FAO/RC/CRC.14/1/Add.1

Distr.: General
21 June 2018

English only

Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade

Chemical Review Committee
Fourteenth meeting
Rome, 11–14 September 2018
Item 2 (b) of the provisional agenda*

Organizational matters: organization of work

Annotations to the provisional agenda

Item 1

Opening of the meeting

1. The fourteenth meeting of the Chemical Review Committee will be held at the headquarters of the Food and Agriculture Organization of the United Nations, Rome, from 11 to 14 September 2018. The meeting will be opened by the Chair of the Committee, Ms. Noluzuko Gwayi (South Africa), at 2 p.m. on Tuesday, 11 September 2018.

2. Opening and welcoming statements will be delivered.

Item 2

Organizational matters

(a) Adoption of the agenda

3. The Committee may wish to adopt its agenda, with any amendments, on the basis of the provisional agenda (UNEP/FAO/RC/CRC.14/1).

(b) Organization of work

4. The Committee has before it a scenario note for the meeting prepared by the Chair (UNEP/FAO/RC/CRC.14/INF/1) and a tentative schedule for the meeting prepared by the Secretariat (UNEP/FAO/RC/CRC.14/INF/2).

5. The Committee may wish to meet on Tuesday, 11 September 2018 from 2 p.m. to 5 p.m. and from Wednesday, 12 September to Friday, 14 September from 9.30 a.m. to 12.30 p.m. and from 2 p.m. to 5 p.m., subject to adjustments as necessary.

6. The Committee may wish to establish contact groups and drafting groups, as necessary, and specify their mandates.

Item 3

Rotation of the membership

7. The Committee has before it a note by the Secretariat on the rotation of the membership and experts nominated as members of the Chemical Review Committee (UNEP/FAO/RC/CRC.14/INF/3). The Committee may wish to take note of the information provided.

* UNEP/FAO/RC/CRC.14/1.

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Item 4
Technical work

(a) Consideration of draft decision guidance documents

(i) Acetochlor

8. The Committee has before it a note by the Secretariat containing a draft decision guidance document for acetochlor, available in the six official languages of the United Nations (UNEP/FAO/RC/CRC.14/3). A tabular summary of comments on the draft decision guidance document is available in document UNEP/FAO/RC/CRC.14/INF/6. The Committee may wish to finalize the draft decision guidance document and to forward it, together with its recommendation to list acetochlor in Annex III to the Convention as a pesticide, for consideration by the Conference of the Parties at its ninth meeting.

(ii) Hexabromocyclododecane

9. The Committee has before it a note by the Secretariat containing a draft decision guidance document for hexabromocyclododecane, available in the six official languages of the United Nations (UNEP/FAO/RC/CRC.14/4). A tabular summary of comments on the draft decision guidance document is available in document UNEP/FAO/RC/CRC.14/INF/7. The Committee may wish to finalize the draft decision guidance document and to forward it, together with its recommendation to list hexabromocyclododecane in Annex III to the Convention as an industrial chemical, for consideration by the Conference of the Parties at its ninth meeting.

(iii) Phorate

10. The Committee has before it a note by the Secretariat containing a draft decision guidance document for phorate, available in the six official languages of the United Nations (UNEP/FAO/RC/CRC.14/5). A tabular summary of comments on the draft decision guidance document is available in document UNEP/FAO/RC/CRC.14/INF/8. The Committee may wish to finalize the draft decision guidance document and to forward it, together with its recommendation to list phorate in Annex III to the Convention as a pesticide, for consideration by the Conference of the Parties at its ninth meeting.

(b) Report of the Bureau on the preliminary review of notifications of final regulatory action

11. The Committee has before it a note by the Secretariat setting out the report of the Bureau on the preliminary review of notifications of final regulatory action (UNEP/FAO/RC/CRC.14/2). In addition, information on trade in chemicals under consideration by the Chemical Review Committee and a summary record of notifications of final regulatory action for chemicals reviewed by the Interim Chemical Review Committee and the Chemical Review Committee are available in documents UNEP/FAO/RC/CRC.14/INF/4 and UNEP/FAO/RC/CRC.14/INF/5 respectively. The Committee may wish to proceed with the review of the notifications of final regulatory action and the supporting documentation before it as suggested in document UNEP/FAO/RC/CRC.14/2.

(c) Review of notifications of final regulatory action

(i) Hexabromocyclododecane

12. The Committee has before it a note by the Secretariat containing a notification of final regulatory action relating to hexabromocyclododecane in the industrial chemical category from one prior informed consent region: North America (Canada) (UNEP/FAO/RC/CRC.14/6). The supporting documentation provided by Canada is set out in document UNEP/FAO/RC/CRC.14/INF/9. This notification was received subsequent to the thirteenth meeting of the Committee and is in addition to previous notifications of final regulatory action received relating to this chemical.

13. At its thirteenth meeting, the Chemical Review Committee decided that notifications related to hexabromocyclododecane from the Asian (Japan) and European (Norway) prior informed consent regions met all the criteria of Annex II to the Convention and accordingly recommended to the Conference of the Parties that hexabromocyclododecane be listed in Annex III to the Convention as an industrial chemical. The notifications from Japan and Norway and the rationale for the recommendation are set out in document UNEP/FAO/RC/CRC.14/INF/10.

14. The Committee may wish to review the information provided in those documents and consider the action proposed in document UNEP/FAO/RC/CRC.14/6.

(ii) Methyl parathion

15. The Committee has before it a note by the Secretariat containing a notification of final regulatory action relating to methyl parathion in the pesticide category from one prior informed consent region: Latin America and the Caribbean (Panama) (UNEP/FAO/RC/CRC.14/7). The supporting documentation provided by Panama is set out in document UNEP/FAO/RC/CRC.14/INF/11.

16. At its first meeting, the Chemical Review Committee decided that a notification related to methyl parathion in the pesticide category from the European prior informed consent region (European Community) met all the criteria of Annex II to the Convention. The notification from the European Community and the rationale for the recommendation are set out in document UNEP/FAO/RC/CRC.14/INF/12.

17. The Committee may wish to review the information provided in those documents and consider the action proposed in document UNEP/FAO/RC/CRC.14/7.

(iii) Perfluorooctanoic acid (PFOA), its salts and PFOA-related compounds

18. The Committee has before it a note by the Secretariat containing notifications of final regulatory action relating to perfluorooctanoic acid (PFOA), its salts and PFOA-related compounds in the industrial chemicals category from two prior informed consent regions: Europe (Norway) and North America (Canada) (UNEP/FAO/RC/CRC.14/8). The supporting documentation provided by Norway and Canada is set out in documents UNEP/FAO/RC/CRC.14/INF/13 and UNEP/FAO/RC/CRC.14/INF/14 respectively. The Committee may wish to review the information provided in those documents and consider the action proposed in document UNEP/FAO/RC/CRC.14/8.

Item 5

Updates to the Handbook of Working Procedures and Policy Guidance for the Chemical Review Committee

19. The Committee has before it a note by the Secretariat on updates to the Handbook of Working Procedures and Policy Guidance for the Chemical Review Committee (UNEP/FAO/RC/CRC.14/9). The Committee may wish to take note of the information provided in those documents and consider the action proposed in document UNEP/FAO/RC/CRC.14/9.

Item 6

Venue and date of the fifteenth meeting of the Committee

20. The Committee may wish to consider and reach agreement on the venue and date of its fifteenth meeting.

Item 7

Other matters

21. The Committee has before it a note by the Secretariat including a collection of examples of severely hazardous pesticide proposals reviewed by the Committee in the past (UNEP/FAO/RC/CRC.14/INF/15). The Committee may wish to take note of the information provided therein.

22. The Committee may also wish to consider any other matters raised by its members during the course of the meeting.

Item 8

Adoption of the report

23. The Committee will be invited to consider and adopt the draft report of the meeting prepared by the rapporteur.

Item 9

Closure of the meeting

24. It is expected that the Chair will close the meeting by 5 p.m. on Friday, 14 September 2018.

UNITED NATIONS

UNEP

Food and Agriculture Organization of the United Nations

RC

UNEP/FAO/RC/CRC.14/2

Distr.: General
15 May 2018

English only

Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade

Chemical Review Committee
Fourteenth meeting
Rome, 11–14 September 2018
Item 4 (b) of the provisional agenda*

Technical work: report of the Bureau on the preliminary review of notifications of final regulatory action

Report of the Bureau on the preliminary review of notifications of final regulatory action

Note by the Secretariat

I. Introduction

1. By its decision RC-2/2, the Conference of the Parties to the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade adopted a process for the preparation of draft decision guidance documents, which was subsequently amended by decisions RC-6/3 and RC-7/3. In accordance with the process, task groups are to be established for chemicals and severely hazardous pesticide formulations scheduled for consideration by the Chemical Review Committee. For ease of reference, the procedure is set out in a handbook of working procedures and policy guidance for the Chemical Review Committee.[1]

2. In accordance with the procedure, the Bureau of the Committee undertook a preliminary review of the notifications of final regulatory action to be reviewed by the Committee at its fourteenth meeting. The report of the Bureau on its preliminary review, including recommendations on the establishment of task groups, is set out in the annex to the present note, without formal editing.

II. Proposed action

3. The Committee may wish to take note of the report of the Bureau on its preliminary review.

* UNEP/FAO/RC/CRC.14/1.

[1] http://www.pic.int/TheConvention/ChemicalReviewCommittee/Guidance/tabid/1060/language/en-US/Default.aspx.

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Annex

[to be inserted]

UNITED NATIONS

UNEP

Food and Agriculture Organization of the United Nations

RC

UNEP/FAO/RC/CRC.14/3*

Distr.: General
25 May 2018

Original: English

Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade

Chemical Review Committee
Fourteenth meeting
Rome, 11–14 September 2018
Item 4 (a) (i) of the provisional agenda**

Technical work: consideration of draft decision guidance documents: acetochlor

Draft decision guidance document for acetochlor

Note by the Secretariat

I. Introduction

1. At its thirteenth meeting, the Chemical Review Committee reviewed notifications of final regulatory action for acetochlor submitted by the European Union and 10 African parties – Burkina Faso, Cabo Verde, Chad, the Gambia, Guinea-Bissau, Mali, Mauritania, the Niger, Senegal and Togo – together with the supporting documentation referenced therein, and concluded that the notifications met all the criteria of Annex II to the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade.

2. In its decision CRC-13/1, the Committee recommended that the Conference of the Parties list acetochlor in Annex III to the Convention as a pesticide. In the same decision, the Committee adopted a rationale for its conclusions, decided to prepare a draft decision guidance document for acetochlor and also decided on the composition of the intersessional drafting group to prepare the document. A detailed workplan for the development of the decision guidance document was prepared by the Committee, in line with the process adopted by the Conference of the Parties by decision RC-2/2 and amended by decisions RC-6/3 and RC-7/3. The recommendation, rationale and workplan were annexed to the report of the Committee on the work of its thirteenth meeting (UNEP/FAO/RC/CRC.13/19, annexes I and III).

3. The material available to the intersessional drafting group included a summary of the outcome of the thirteenth meeting of the Committee, a copy of the working paper on the preparation of internal proposals and decision guidance documents for banned and severely restricted chemicals and the notifications of final regulatory action and associated supporting documentation available to the Committee at its thirteenth meeting.

4. In accordance with the agreed workplan, Ms. Parvoleta Angelova Luleva (Germany), the chair of the intersessional drafting group, and Ms. Leonarda Christina van Leeuwen (Netherlands), the vice-chair, prepared an internal proposal based on the notifications and the supporting documentation. That internal proposal was circulated to the members of the drafting group for comment on 14 December 2017. It was amended in the light of the comments received and was circulated on 16 February 2018 to all Committee members and to the observers who had attended the thirteenth meeting. Responses were received from Committee members and observers and taken into consideration in the preparation of the draft decision guidance document.

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* Reissued for technical reasons on 06 August 2018.

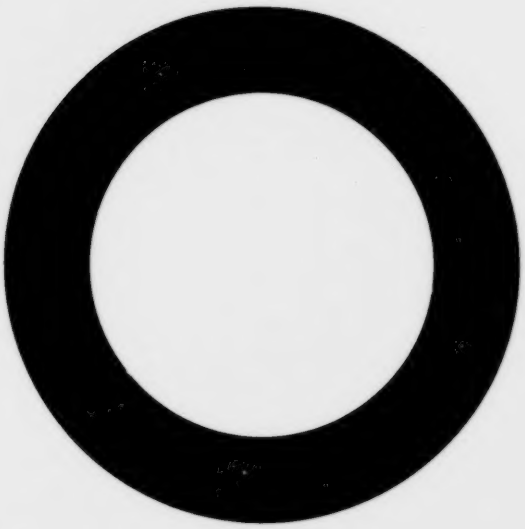
** UNEP/FAO/RC/CRC.14/1.

5. The draft decision guidance document and a compilation of the comments received were circulated to the members of the drafting group on 27 April 2018.

6. The text of the draft decision guidance document, as submitted by the drafting group, is set out in the annex to the present note. It has not been formally edited. A tabular summary of the comments received, including information on how they were addressed, is set out in the annex to the note by the Secretariat on the matter (UNEP/FAO/RC/CRC.14/INF/6).

II. Proposed action

7. The Committee may wish to finalize the draft decision guidance document and to forward it, together with its recommendation to list acetochlor in Annex III to the Convention as a pesticide, for consideration by the Conference of the Parties at its ninth meeting.



Annex

Rotterdam Convention

Operation of the prior informed consent procedure for banned or severely restricted chemicals

Draft Decision Guidance Document

Acetochlor

Secretariat of the Rotterdam Convention
on the Prior Informed Consent Procedure
for Certain Hazardous Chemicals and Pesticides
in International Trade

Food and Agriculture
Organization of the
United Nations

UNEP

Disclaimer

The use of trade names in the present document is primarily intended to facilitate the correct identification of the chemical. It is not intended to imply any approval or disapproval of any particular company. As it is not possible to include all trade names presently in use, only a number of commonly used and published trade names have been included in the document.

While the information provided is believed to be accurate according to data available at the time of preparation of the present decision-guidance document, FAO and UNEP disclaim any responsibility for omissions or any consequences that may arise there from. Neither FAO nor UNEP shall be liable for any injury, loss, damage or prejudice of any kind that may be suffered as a result of importing or prohibiting the import of this chemical.

The designations employed and the presentation of material in this publication do not imply the expression of any opinion whatsoever on the part of FAO or UNEP concerning the legal status of any country, territory, city or area or of its authorities or concerning the delimitation of its frontiers or boundaries.

Standard core set of abbreviations[3]

STANDARD CORE SET OF ABBREVIATIONS	
<	less than
≤	less than or equal to
>	greater than
≥	greater than or equal to
µg	microgram
µm	micrometre
ARfD	acute reference dose
a.i.	active ingredient
ADI	acceptable daily intake
AOEL	acceptable operator exposure level
b.p.	boiling point
bw	body weight
°C	degree Celsius (centigrade)
CAS	Chemical Abstracts Service
cc	cubic centimetre
cm	centimetre
DNA	deoxyribose nucleic acid
DT_{50}	dissipation time 50%
EC	European Community
EC_{50}	median effective concentration
ED_{50}	median effective dose
EEC	European Economic Community
EHC	Environmental Health Criteria
EU	European Union
EFSA	European Food Safety Authority
FAO	Food and Agriculture Organization of the United Nations
g	gram
h	hour
ha	hectare
i.m.	intramuscular
i.p.	intraperitoneal
IARC	International Agency for Research on Cancer
IC_{50}	median inhibitory concentration
ILO	International Labour Organization
IPCS	International Programme on Chemical Safety
IPM	Integrated Pest Management
IUPAC	International Union of Pure and Applied Chemistry
JMPR	Joint FAO/WHO Meeting on Pesticide Residues (Joint Meeting of the FAO Panel of Experts on Pesticide Residues in Food and the Environment and a WHO Expert Group on Pesticide Residues)

[3] *This core list should serve as the basis for DGDs for industrial chemicals, pesticides and severely hazardous pesticide formulations. It should be augmented by abbreviations used in the individual DGDs relevant to the chemical(s) in question.*

Definitions and spelling should, as far as practicable, follow the IUPAC glossary of terms in toxicology and the IUPAC glossary of terms relating to pesticides in their current editions.

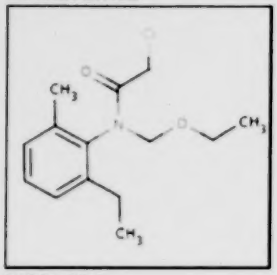
As a general rule it is preferable that acronyms used only once in the text be spelled out rather than included in the list of abbreviations.

STANDARD CORE SET OF ABBREVIATIONS	
k	kilo- (x 1000)
kg	kilogram
Koc	soil organic partition coefficient.
Kow	octanol–water partition coefficient
kPa	kilopascal
L	litre
LC_{50}	median lethal concentration
LD_{50}	median lethal dose
LOAEL	lowest-observed-adverse-effect level
LOEL	Lowest-observed-effect level
m	metre
m.p.	melting point
mg	milligram
ml	millilitre
mPa	millipascal
MRL	maximum residue limit
MTD	Maximum Tolerated Dose
ng	nanogram
NOAEC	no-observed-adverse-effect concentration
NOAEL	no-observed-adverse-effect level
NOEC	no-observed-effect concentration
NOEL	no-observed-effect level
OECD	Organisation for Economic Co-operation and Development
PEC	predicted environmental concentration
Pow	octanol-water partition coefficient, also referred to as Kow
PPE	personal protective equipment
ppm	parts per million (used only with reference to the concentration of a pesticide in an experimental diet. In all other contexts the terms mg/kg or mg/L are used).
RAC	Risk Assessment Committee of the European Chemicals Agency
RMS	Rapporteur Member State
RfD	reference dose (for chronic oral exposure; comparable to ADI)
SMR	standard(ized) mortality ratio
STEL	short-term exposure limit
TER	toxicity exposure ratio
TLV	threshold limit value
TWA	time-weighted average
UNEP	United Nations Environment Programme
USEPA	United States Environmental Protection Agency
UV	ultraviolet
VOC	volatile organic compound
w/w	weight for weight
WHO	World Health Organization
wt	weight

Decision guidance document for a banned or severely restricted chemical

Acetochlor **Published:**

1. Identification and uses (see Annex 1 for further details)

Common name	acetochlor
Chemical name and other names or synonyms	**IUPAC:** 2-chloro-N-ethoxymethyl-6'-ehtylacet-*o*-toluidide **CA:** 2-chloro-N-(ethoxymethyl)-N-(2-ethyl-6-methylphenyl)acetamide
Molecular formula	C14H20ClN02
Chemical structure	
CAS-No.(s)	34256-82-1
Harmonized System Customs Code	2924.29
Other numbers	**EINECS:** 251-899-3
Category	Pesticide
Regulated category	Pesticide
Use(s) in regulated category	Acetochlor has been used in the European Union as a herbicide on maize to control weeds through broadcast spraying. Acetochlor has been used as a selective herbicide on maize in the CILSS countries.
Trade names	Trade names listed by the EU: Acenit, Guardian, Harness, Relay, Sacemid, Surpass, Top-Hand, Trophy and Winner Trade names listed by the Burkina Faso, Cabo Verde, Chad, the Gambia, Guinea-Bissau, Mali, Mauritania, the Niger, Senegal and Togo: ACEDAF 400 EC, ACEPROMAÏS 400 SC, ACEPRONET 400 EC, ACETO 900 EC, ACETOCAL 900 EC, HERBISUPER KEYTOCHLORE 900 EC *This is an indicative list. It is not intended to be exhaustive.*
Formulation types	Capsule suspension (CS), Emulsifiable concentrate (EC) *This is an indicative list. It is not intended to be exhaustive.*
Uses in other categories	None
Basic manufacturers	Dow AgroSciences, Monsanto Service International S.A *This is an indicative list of current and former manufacturers. It is not intended to be exhaustive.*

2. Reasons for inclusion in the PIC procedure

Acetochlor is included in the PIC procedure as a pesticide. It is listed on the basis of the final regulatory actions taken by Burkina Faso, Cabo Verde, Chad, the Gambia, Guinea-Bissau, Mali, Mauritania, the Niger, Senegal, Togo (hereafter referred to as the CILSS countries) and the European Union to ban the use of acetochlor as a pesticide.

No final regulatory actions relating to uses as industrial chemical have been notified.

2.1 Final regulatory action (see Annex 2 for further details)

CILSS countries

The ten Parties from the African region are members of the Sahelian Pesticides Committee. As the members of the Committee work together to take decisions on the registration of pesticides on a regional basis, the notifications submitted by these Parties refer to the same final regulatory action.

Decision N°002/MC/2017 bans all products containing acetochlor and entered into force on 20 March 2017. The import, manufacture for domestic use, distribution and sale have also been banned.

Reason: Human health and the environment

European Union

It is prohibited to place on the market or use plant protection products containing acetochlor in the European Union (Commission Implementing Regulation (EU) No 1372/2011 of 21 December 2011 concerning the non-approval of the active substance acetochlor, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending Commission Decision 2008/934/EC (Official Journal of the European Union L 341, 22.12.2011, p. 45-46)). Acetochlor is not approved for placing on the market pursuant to Regulation (EC) No. 1107/2009 concerning the placing of plant protection products on the market (which replaces Directive 91/414/EEC). All authorisations for plant protection products containing acetochlor had to be withdrawn by the Member States by 23 June 2012 and all uses of plant protection products containing acetochlor are prohibited as of 23 June 2013 at the latest.

Reason: Human health and the environment

2.2 Risk evaluation (see Annex 1 for further details)

CILSS countries

The final regulatory action (Decision N 002/MC/2017) to ban all products containing acetochlor in the Sahel countries was based on a risk evaluation and took into account scientific information from a variety of sources.

The CILSS countries found that acetochlor caused great difficulties for users in the CILSS countries to use acetochlor without unacceptable risk to human health and the environment. The risks to human health (by contamination of groundwater and surface water which are both used as drinking water), operators (due to the absence of sufficient personal protection measures) and to the environment (due to the intrinsic properties of the substance, the risk of water contamination and the specific conditions in the Sahel) make it difficult to use acetochlor safely.

The risk evaluation took into account the conditions within the notifying Parties, for example the conditions of application of the substance, the availability of personal protective equipment, and the regional environmental circumstances and identified the following concerns:

Human health

- Potential risk for human exposure through surface and ground water contamination by the metabolite t-norchloro acetochlor, which is genotoxic[4]: ground water is used as drinking water reservoir for humans and surface water is used as drinking water for humans and animals;
- Difficulties for the population in finding suitable personal protective equipment;
- Absence of an environmental management system respecting buffer strips between treated fields and streams. Since this precaution is not possible in the Sahel, the use of acetochlor entails an unacceptable risk to human health and the environment.

Environment

- High risk of surface and groundwater contamination by acetochlor and its metabolites;
- High risk to non-target terrestrial plants;
- Long term high risk to herbivorous birds;
- Surface water contamination and high risk to aquatic organisms;
- High short-term risk to birds drinking contaminated water following post emergence treatment;
- The fragile ecology of CILSS countries, sometimes characterised by torrential rainfall on soils which are very often poor in organic matter and therefore subject to erosion and leaching;

[4] Conclusion from CILSS countries based on EFSA (2011), which indicates that t-norchloro acetochlor (t-NCA) has genotoxic potential. In the EFSA review, 4 studies on the genotoxicity of t-NCA were cited, one showing doubtful, one showing positive and one showing negative results. Also see Annex 1 section 2.2.3

- Risk of soil impoverishment in the Sahel;
- Absence of an environmental management system respecting buffer strips between treated fields and streams. Since this precaution is not possible in the Sahel, the use of acetochlor entails an unacceptable risk to human health and the environment.

European Union

A risk assessment was carried out on the basis of Directive 91/414/EEC (replaced by Regulation (EC) No 1107/2009), which provides for the European Commission to issue a work programme for the examination of existing active substances used in plant protection products with a view to their possible inclusion in Annex I to the Directive, and in accordance with the provisions of Regulation (EC) No 1095/2007 and Regulation (EC) No 2229/2004. A Member State was designated to undertake the risk assessment based on the information submitted by the applicant and to establish a draft assessment report, which was subject to peer review during which the European Food Safety Authority (EFSA) undertook consultations with experts from Member States as well as with the applicant.

The EU risk assessment took into account the proposed conditions of use of acetochlor within the EU, including the intended uses, recommended application rates and good agricultural practices. The conclusion on the peer review was reached on the basis of the evaluation of the notified representative uses as an herbicide on maize in the EU.

For some criteria in the risk evaluation, it was not demonstrated that the risks were acceptable due to the lack of information; in particular the information available was not sufficient to conclude on the risk assessment for the groundwater contamination for metabolites t-norchloroacetochlor and t-hydroxyacetochlor.

However, evaluations made by the designated RMS and EFSA on the basis of the available information demonstrated that the following concerns for human health and the environment were identified under the proposed conditions of use in the EU:

Human health

- The potential human exposure is above 100% of the ADI when predicted concentrations of the ground water metabolites t-oxanilic acid, t-sulfinylacetic acid, t-sulfonic acid and s-sulfonic acid that have been concluded as relevant metabolites are taken into account.
- There is a potential human exposure to metabolite t-norchloro acetochlor when surface water is abstracted for drinking water, which has been concluded as relevant from a toxicological hazard assessment perspective. In addition, the toxicological data for t-norchloro acetochlor indicate that it is genotoxic.
- A high potential for groundwater contamination has been identified over significant areas of the EU by the metabolites t-oxanilic acid, t-sulfinylacetic acid, t-sulfonic acid and s-sulfonic acid, which have been concluded as relevant metabolites.
- No valid method has been available to quantify residues in food of plant origin.

Environment

- Acetochlor is very toxic to all groups of aquatic organisms and there is a high risk to aquatic organisms.
- A high acute risk to birds from uptake of contaminated drinking water was indicated for the post emergence applications.
- There is a high risk to non-target terrestrial plants. The risk assessment suggests that an in-field no spray buffer zone of 5m is required to protect non target plants in the off-field area.
- A high long term risk for herbivorous birds has been identified.

3. Protective measures that have been applied concerning the chemical

3.1 Regulatory measures to reduce exposure

CILSS countries	The final regulatory action of the Parties bans the use of acetochlor as an active ingredient in plant protection products. The final regulatory actions are expected to lead to a significant decrease in the quantity of the chemical used, resulting in significant reduction of the exposure of humans and the environment. The reduction in exposure to the chemical will lead to reduction of risk caused by acetochlor to human health and the environment.
European Union	The final regulatory action of the Parties bans the use of acetochlor as an active ingredient in plant protection products. The final regulatory actions are expected to lead to a significant decrease in the quantity of the chemical used, resulting in significant reduction of the exposure of humans and the environment. The reduction in exposure to the chemical will lead to reduction of risk caused by acetochlor to human health and the environment.

3.2 Other measures to reduce exposure

CILSS countries

Not reported

European Union

Not reported

3.3 Alternatives

There are a number of alternative methods involving chemical and non-chemical strategies, including alternative technologies available, depending on the individual crop-pest complex under consideration. Countries should consider promoting, as appropriate, integrated pest management (IPM) and organic strategies as a means of reducing or eliminating the use of hazardous pesticides.

CILSS countries

1. Chemical alternatives

Alternatives to the use of acetochlor based formulations exist. Formulations of selective pesticides are registered and authorised for sale in CILSS countries. Several selective pesticides formulations can be found in the global list of pesticides registered by CSP for maize and cotton. (CSP, 2016, website: www.insah.org). These formulations belong to the following chemical classes: sulfonylurea (nicosulfuron), substituted ureas (diuron), toluidin (pendimethalin), etc.

2. Integrated production and pest management (IPPM)

IPPM experience initiative launched by FAO in collaboration with the Ministers of Agriculture in several Sahel countries allowed obtaining important results in agricultural production and pest management. This initiative of development and implementation of good agricultural practices (GAPs) allows to enhance agricultural productivity and to train several farmers as potential facilitators.

European Union

Not reported

3.4 Socio-economic effects

CILSS countries

No assessment of socio-economic effects was reported.

European Union

No assessment of socio-economic effects was reported.

4. Hazards and Risks to human health and the environment

4.1 Hazard Classification	
WHO / IPCS	III (slightly hazardous)
IARC	Not available
European Union	**Classification of the EU according to Regulation (EC) No 1272/2008 of the European Parliament and of the Council, as adopted pursuant to Commission Regulation (EU) 2016/1179** Carc. 2 - H351 (Suspected of causing cancer) Repr. 2 - H361f (Suspected of damaging fertility) Acute Tox. 4 - H332 (Harmful if inhaled) STOT SE 3 - H335 (May cause respiratory irritation) STOT RE 2 - H373 (kidney) May cause damage to organs through prolonged or repeated exposure Skin Irrit. 2 - H315 (Causes skin irritation) Skin Sens. 1 - H317 (May cause an allergic skin reaction) Aquatic Acute 1 - H400 (Very toxic to aquatic life) Aquatic Chronic 1 H410 (Very toxic to aquatic life with long lasting effects) (EU notification) *Reference: https://echa.europa.eu/information-on-chemicals/cl-inventory-database/-/discl/details/104340, accessed 26 April 2018*
US EPA	oral, dermal and eye irritation – III inhalation – IV dermal irritation – II and found to be a dermal sensitizer
Japan	According to the GHS classification approved by Japan, this substance is Carcinogenic category 1B, Reprotoxic category 2, Specific target organ toxicity – Repeated exposure : Category 1 (kidney, testis), Category 2 (central nervous system), Hazardous to the aquatic environment (acute and long-term) category 1 *Reference: http://www.safe.nite.go.jp/english/ghs/11-mhlw-00096e.html, accessed 26 April 2018*

4.2 Exposure limits

No internationally recognised exposure limits are available for this chemical. National exposure limits from the notifying countries are presented in Annex II.

4.3 Packaging and labelling	
The United Nations Committee of Experts on the Transportation of Dangerous Goods classifies the chemical in:	
Hazard Class and Packing Group:	Based on UN number 3082; Hazard class 9, UN Packing group III
International Maritime Dangerous Goods (IMDG) Code	Based on UN number 3082; Hazard class 9, UN Packing group III
Transport Emergency Card	Not available
Further specific guidance on appropriate symbols and label statements for acetochlor products may be available in the FAO Guidelines on Good Labelling Practice for Pesticides.	

4.4 First aid

Not available

NOTE: The following advice is based on information available from the World Health Organisation and the notifying countries and was correct at the time of publication. This advice is provided for information only and is not intended to supersede any national first aid protocols.

4.5 Waste management

Not available

Annexes

Annex 1	**Further information on the chemical**
Annex 2	**Details on final regulatory actions reported**
Annex 3	**Addresses of designated national authorities**
Annex 4	**References**

Annex 1 Further information on the chemical

Introduction

The information presented in this Annex reflects the conclusions of the notifying parties: Burkina Faso, Cabo Verde, Chad, the Gambia, Guinea-Bissau, Mali, Mauritania, the Niger, Senegal, Togo and the European Union. These notifications were published in PIC Circular XLV of June 2017.

Relevant information from WHO and FAO (JMPR, 2015) is included in the section 2.2.3 on genotoxicity (including mutagenicity) and 2.2.4 on long-term toxicity and carcinogenicity of this Annex. The JMPR report is from a more recent date (2015) than the information from the notifying countries and provides a different view on the genotoxicity and carcinogenicity of acetochlor.

Where possible, information on hazards provided by the notifying parties has been presented together, while the evaluation of the risks, which are specific to the conditions prevailing in the notifying Parties are presented separately.

1. Identity and Physico-Chemical properties

1.1	**Identity**	ISO: Acetochlor IUPAC: 2-chloro-N-ethoxymethyl-6'-ethylacet-*o*-toluidide CA: 2-chloro-N-(ethoxymethyl)-N-(2-ethyl-6-methylphenyl)acetamide
1.2	**Formula**	C14H20ClNO2
1.3	**Colour and Texture**	Pure material: pale yellow, free-flowing liquid (99.9%) Technical material: pale yellow, free-flowing liquid (95.0%)
1.4	**Decomposition temperature**	237-239°C (at 98.78 KPa) (99.9 %)
1.6	**Density (g/cm³)**	1.136 g/mL at 20 deg C; 1.107 g/mL at 25 deg C; 1.1 g/mL at 30 deg C
1.7	**Resistance to acids**	No information available.
1.8	**Resistance to alkalis**	No information available.
1.9	**Tensile strength (10^3 kg/cm²)**	No information available.

2 Toxicological properties

2.1	**General**	
2.1.1	**Mode of Action**	**CILSS Countries** Elongase inhibition, and inhibition of geranylgeranyl pyrophosphate (GGPP) cyclization enzymes, part of the gibberellin pathway. (Footprint PPDB, 2015; INERIS, 2013; (CILSS notification) Produces tumors of the nasal olfactory epithelium in rats by way of a non-linear, non-genotoxic mode of action that includes cytotoxicity of the olfactory epithelium, followed by regenerative cell proliferation of the nasal epithelium that can then lead to neoplasia if cytotoxicity and proliferation are sustained. Produces tumors of the thyroid follicular cells in rats by way of a non-genotoxic mode of action that includes UDPGT induction, increased TSH, alterations in T3/T4 hormone production and thyroid hyperplasia. (The Grouping of a Series of Chloroacetanilide Pesticides Based on a Common Mechanism of Toxicity (USEPA 2006) (CILSS notification).
2.1.2	**Symptoms of poisoning**	**CILSS Countries** Minor effects to the eyes and skin; No recommendations are made based on the limited information available. (US EPA, 2009) (CILSS notification).

2.1.3 Absorption, distribution, excretion and metabolism in mammals

Oral absorption is rapid and almost complete, based on urine and bile excretion in rat being >80% following repeated dosing at 10 mg/kg bw/day. It is widely distributed in the body but the potential for accumulation is low, although there is some accumulation in nasal turbinates in rat (but not in mice). The rate of excretion is relatively rapid (~86% within 48 hours), mainly in urine (66-72%) and in faeces (12-21%, of which 80-85% comes via the bile). Acetochlor undergoes conjugation and mixed function oxygenation with the main metabolite in rat and monkey being *tert*-mercapturic acid with 25-27% of the radioactivity excreted in monkey urine. (EFSA, 2011) (EU notification).

2.2 Toxicology studies

2.2.1 Acute toxicity

European Union

The acute toxicity of acetochlor after oral or inhalative administration is moderate (LD_{50} rats, oral = 1929 mg/kg body weight, LC_{50} rats, inhalation = 3.99 mg/l/4 h (exposure nose-only, test material aerosol)). It is irritating for the respiratory system and for the skin, as well as a skin sensitiser (LD_{50} (rat, dermal): >2000 mg/kg bw) (EFSA, 2011).

Acetochlor based formulations registered by CSP belong to WHO class III (moderately harmful) (CSP, 2014).

2.2.2 Short term toxicity

European Union

Three dietary studies in rats, four oral studies (dietary and capsules) in dog and two dermal studies in rats and rabbits are described. The dog is the most sensitive species with a NOAEL (52 -week dog study) of 2 mg/kg bw/d based on decreased body weight gain and histopathological findings in kidneys and testes observed at 10 mg/kg bw/day (EFSA, 2011).

2.2.3 Genotoxicity (including mutagenicity)

European Union

Positive and negative results have been reported *in vivo* and *in vitro* with technical material of low and high purity (from 89.9 to 96.7 %). Many *in vitro* studies show positive results. The *in vivo* UDS test shows positive results at toxic dose levels and clear negative results are found in micronucleus and dominant lethal studies. Experts agreed that the substance induces DNA repair synthesis *in vivo*, which was not considered as a clear indication of mutagenicity *in vivo* and they concluded that this does not affect the risk assessment (EFSA, 2011).

Genotoxicity of the metabolite t-norchloro acetochlor

The following studies are summarized in EFSA (2011):

Assay	Species	Result
In vitro gene mutation	Bacterial cells	Doubtful results in first assay
In vitro gene mutation	Mouse lymphoma cells	Positive
In vitro chromosome aberrations	Human lymphocytes	Negative (+/- S9)
In vitro chromosome aberrations	Mouse (micronucleus test)	Negative

It was concluded that "the groundwater metabolite t-norchloro acetochlor (6) is also toxicologically relevant based on its genotoxic (see table above) and carcinogenic potential (from acetochlor), and no reference values were agreed" (EFSA 2011).

WHO and FAO

Results for gene mutation assays are conflicting and provide no clear evidence of a positive effect in either bacterial or mammalian cell test systems. Similarly, the evidence from in vitro and in vivo unscheduled DNA synthesis assays, in vitro sister chromatid exchange studies and an in vivo comet test provides no convincing pattern of genotoxic activity. By contrast, results from chromosomal aberration assays indicate that acetochlor is a confirmed clastogen in cultured human lymphocytes. There is also the possibility that the increased mutant colony counts observed in the positive mouse lymphoma assay resulted from a clastogenic rather than a mutagenic response, as this test system can detect chromosome breakage. Nevertheless, clastogenicity is confined to in vitro mammalian cell test systems, and the types of induced aberrations suggest cytotoxicity. Based on data from three bone marrow assays and three dominant

lethal mutation studies in mice or rats, acetochlor-induced clastogenicity is not expressed in either somatic or germinal cells of whole animals (JMPR, 2015).

Genotoxicity of the metabolite t-norchloro acetochlor

In the JMPR report from 2015, the following studies are summarized:

Study	Test system	Purity (%)	Results	Reference
Bacterial gene mutation (Ames)	S. typhimurium TA98, TA100, TA1535 and TA1537; E. coli WP2 and WP2P uvrA	99.5	Negative	Callander (2002)
Bacterial gene mutation (Ames)	S. typhimurium TA98, TA100, TA1535 and TA1537; E. coli WP2 and WP2P uvrA	99	Negative	Wagner (2013)
In vitro mammalian gene mutation	Mouse lymphoma	99.5	Weakly positive (up to 2.6 times control)	Clay (2002)
In vitro chromosomal aberration	Human lymphocytes	99.5	Negative	Fox (2002)
In vivo micronucleus	Mouse (bone marrow)	99.5	Negative	Fox (2002b)
In vivo transgenic gene mutation	Mouse	> 99	Negative	Beevers (2014)

It was concluded that "No evidence of genotoxicity was observed in various in vivo and in vitro assays, except for a mouse lymphoma assay, which gave a weak positive response for two metabolites; however, these two metabolites were negative in a mouse micronucleus assay.

The Meeting concluded that these plant metabolites, soil degradates and environmental metabolites of acetochlor appear to be less toxic than the parent compound." (JMPR, 2015).

2.2.4 Long term toxicity and carcinogenicity

European Union

Long-term toxicity

Target/Critical effects: anaemia, kidney and liver toxicity (mice and rats).
Rat (diet, 2 year): NOAEL = 9.4 mg/kg bw/day
Mouse (diet, 78 week): LOAEL = 1.1 mg/kg bw/day (EFSA, 2011).

Carcinogenicity

Rat: adenomas in nasal epithelium at 47.5 mg/kg bw/day. Gastric tumours.
Mouse: lung adenomas and carcinomas, uterine histocytic sarcomas.
In conclusion, taking into account the different tumours observed in both species, the meeting agreed to propose the classification Carc. cat.3, R40 Limited evidence of a carcinogenic effect. (EFSA, 2011).

WHO and FAO

Rat: Adenomas in nasal epithelium

Mouse: Marginal increase in histiocytic sarcomas

Conclusion: Unlikely to pose a carcinogenic risk to humans from the diet. (JMPR, 2015)

2.2.5	**Effects on reproduction**	**European Union** Reproductive target/critical effect: *Parental*: decreased body weight, increased liver weight, nasal hyperplasia. *Offspring*: reduced litter and pup weight, delayed vaginal opening, increased relative brain weight. *Reproduction*: decreased number of implantations, decreased number of live pups. Relevant parental and offspring NOAEL: 20 mg/kg bw/day Relevant reproductive NOAEL: 61 mg/kg bw/day Developmental target/critical effect: *Maternal*: decreased bodyweight gain, (rat, rabbit), decreased food consumption and increased water consumption (rat). *Developmental*: delayed ossification at maternal toxic dose (rat), none (rabbit). Relevant maternal NOAEL: 200 mg/kg bw/day (rat), 50 mg/kg bw/day(rabbit). Relevant developmental NOAEL: 400 mg/kg bw/day (rat), 190 mg/kg bw/day (rabbit). (EFSA, 2011) The weight of evidence suggests that at high concentrations, acetochlor may affect fertility or reproductive performance in the dog. Smaller effects are seen in the rat 2-generation studies at larger doses than used in the dog studies but it is unclear if the effects in the rat alone are sufficient for classification. The effects on the dog testes are of concern, but it needs to be considered whether the effect is a primary one, i.e. whether acetochlor has a direct toxicological effect on the testes or whether it is secondary to renal insufficiency. The dog studies indicate that this species is the most sensitive. The 1-year dog study by Broadmeadow (1989) also provides evidence for (delayed onset) chronic renal failure (high water consumption, high urinary volume with low specific gravities, increased plasma urea or BUN and creatinine, increased GGT, significant renal histopathology, severe neurological involvement suggestive of uremic toxicity)though not all of the classical effects associated with renal failure are noted (e.g. haematology disturbance, plasma phosphate, calcium and other electrolytes, no decrease in the relative kidney weight). Chronic renal failure is associated with gonadal dysfunction in humans and the same may be true for dogs. There was no investigation of chronic renal failure per se so even the presumption of this diagnosis is a hypothetical one based on the effects noted primarily in a single 12-month dog study with some supporting but weak evidence from the 119-day dog study by Ahmed (1980). In summary, there is sufficient concern to consider classifying acetochlor for its effects on fertility according to CLP. The effects on dog testes at 40-50 mg/kg bw/d in the 1-year studies are severe enough to cause a large reduction in mass and a suspected functional impairment. Furthermore, the 119-day dog study by Ahmed (1980) indicates a trend for a dose-related decrease (but not statistically significant) in testicular weight. There are clear indications of chronic renal failure at the high dose in one 12-month dog study but insufficient evidence to make an association between it and the testicular effects observed. The second 12-month dog study by Ahmed (1981) is more significant because there was no indication of renal failure and no lethalities, but firm evidence for testicular changes was present. There are no mechanistic studies investigating the aetiology of the testicular effects so it is not possible to be certain if they are a consequence of a primary effect by acetochlor or secondary to renal insufficiency. The RAC therefore concluded that acetochlor should be classified as Repr. 2; H361f (RAC, 2014) (Additional information provided by a CRC member from an EU Member State).
2.2.6	**Neurotoxicity/ delayed neurotoxicity, Special studies where available**	**European Union** Acute neurotoxicity: Acute NOAEL = 150 mg/kg bw/day (rat). Repeated dose neurotoxicity: 90-day NOAEL = 48 mg/kg bw/day (rat). Delayed neurotoxicity: No data (EFSA, 2011)
2.2.7	**Summary of mammalian toxicity and overall evaluation**	**European Union** Acetochlor has a moderate acute toxicity. In short term studies the dog was the most sensitive species showing decreased body weight gain and histopathological findings in kidneys and testes. Many in vitro genotoxicity studies showed positive

results but the in vivo tests did not indicate clearly a mutagenic potential. In long term studies different types of tumours were observed with increased incidences. No specific effect on the reproductive parameters was found in multigeneration studies with rats, and no evidence of teratogenicity was observed in rats or rabbits (EFSA, 2011).

Regarding reproduction, the EU Committee for Risk Assessment (RAC), concluded in 2014 that there is sufficient concern to consider classifying acetochlor for its effects on fertility according to CLP (see section 2.2.5) and concluded that the substance should be classified as Reprotoxic category 2 (RAC, 2014) (Additional information provided by CRC member from EU memberstate.

3 Human exposure/Risk evaluation

3.1 Food

European Union

Residues in food of plant origin are analysed using a common moiety method by LC-MS/MS. Data gaps have been identified for validation of the extraction and hydrolysis steps for each metabolite and ILV for the method. Consequently, no valid method is available to quantify residues in food of plant origin. For products of animal origin, a method is not required as no MRLs are proposed.

The acceptable daily intake (ADI) is 0.0036 mg/kg bw/day using the LOAEL from the 78-week mouse study with a safety factor of 300. The acute reference dose (ARfD) is 1.5 mg/kg bw, derived from the acute rat neurotoxicity study with the application of a safety factor of 100.

No chronic or acute risks were identified when the consumer exposures to food commodities are calculated using the EFSA PRIMo Model and the MRL proposed for maize grains and oil seeds; the ADI and ARfD values were not exceeded.

However, it must be highlighted that the potential consumer exposure exceeds the ADI value in many scenarios, when the predicted concentrations of the ground water metabolites are considered. In addition, intakes for toddlers and infants resulting from the water consumption are at times above the threshold value of 20% ADI recommended by the WHO, when calculations are conducted using the concentrations measured in a monitoring program conducted in Northern Italy (EFSA, 2011, EU notification).

WHO and FAO

The Meeting established an ADI of 0–0.01 mg/kg bw on the basis of a NOAEL of 1.10 mg/kg bw per day in the 78-week dietary study in mice, based on slight anaemia and an increased incidence of bronchiolar hyperplasia and interstitial fibrosis in the kidney in males observed at 11.0 mg/kg bw per day. A safety factor of 100 was applied. An ARfD of 1 mg/kg bw was established on the basis of a NOAEL of 100 mg/kg bw per day in a study of developmental toxicity in rabbits, based on decreased feed consumption, decreased body weight (GDs 6–8) and the death of two dams observed at 300 mg/kg bw per day. A safety factor of 100 was applied. (JMPR, 2015).

3.2 Air

European Union

Acetochlor is considered harmful by inhalation (acute rat LC_{50} 3.99 mg/L/4h) (EFSA, 2011).

3.3 Water

European Union

The potential human exposure is above 100% of the ADI when predicted concentrations of the ground water metabolites t-oxanilic acid, t-sulfinylacetic acid, t-sulfonic acid and s-sulfonic acid that have been concluded as relevant metabolites are taken into account.

There is a potential human exposure to metabolite t-norchloro acetochlor when surface water is abstracted for drinking water, which has been concluded as relevant from a toxicological hazard assessment perspective.

A high potential for groundwater contamination has been identified over significant areas of the EU by the metabolites t-oxanilic acid, t-sulfinylacetic acid, t-sulfonic acid and s-sulfonic acid, which have been concluded as relevant metabolites. (EFSA, 2011).

CILSS Countries

In the notification and supporting documentation, risk to human health because of high risk of surface and groundwater contamination by acetochlor and its metabolites is reported.

In the USA, due to concerns for groundwater contamination, acetochlor cannot be used on coarse soils (for ex. Sandy soil with less than 3% of organic matter) where the depth of groundwater in less than 30 feet. Acetochlor cannot be applied with any irrigation system (irrigation by flooding included) nor can it be applied by aerial application. Acetochlor cannot be applied directly on water or in areas where surface water is present. Furthermore, acetochlor must not be mixed or filled less than 50 feet from surface water or wells, unless adequate confinement or disposal measures exist. Each of these measures is intended to prevent acetochlor from migrating to ground water and/or surface water resources (US EPA, 2006).

The supporting documentation from the CILSS countries indicates the absence of an environmental management system respecting buffer strips between treated fields. Since this precaution cannot be implemented in the Sahel, the use of acetochlor entails an unacceptable risk to human health and the environment.

Further, in the CILSS countries, soils are often very poor in organic matter. Modelling values are between 1.06% to 1.36% for soils within the perimeter (Direction culture/SN-SOSUCO,2008), and the mean OC in soils near the rivers is equal to 1.06% (Ouedraogo et al, 2012). Therefore, these soils are subject to erosion and leaching. The fragile ecology of CILSS countries, sometimes characterized by torrential rainfall on soils which are very often poor in organic matter and therefore subject to erosion and leaching.

The results of the modelling study by Ouedraogo et al (2012) conclude that acetochlor had very high potential to contaminate surface water under actual usage conditions in Burkina Faso.

In a study measuring pesticide concentrations in two lakes in Burkina Faso, acetochlor concentrations up to 53.1 µg/L were measured (Soleri, 2013). Contamination of groundwater and surface water in the CILSS countries results in contamination of drinking water, since these are used as sources for drinking water. In countries like Burkina Faso, more than half the farmers (67.5 %) have a water point in their fields or nearby. Most water points are less than 100m from the fields (Toe, 2010). Water pesticide contamination via different routes may result from the proximity of water points to the fields. Water was drunk in 50% of cases, used for the preparation or the dilution of pesticides in 29.26% and for animal drinking in 26.96% (Toe, 2010). Hence the presence of acetochlor in some water courses in Burkina Faso (Soleri, 2013).

The CILSS countries concluded that using acetochlor as a pesticide under these conditions resulted an unacceptable risk to human health because of drinking water contamination.

3.4 Occupational exposure

European Union

The acceptable operator exposure level (AOEL) is 0.02 mg/kg bw/day based on the 1-year dog study, with the use of a safety factor of 100.

Two representative formulations were considered in the exposure assessment. For the formulation 'GF-675', the operator exposure is below the AOEL with the use of gloves and coverall during mixing/loading and application, and sturdy footwear during application. For the formulation 'MON 69447', the estimates with the German and UK models are above the AOEL but a bio-monitoring study measured exposures below the AOEL with the use of tractors and gloves during mixing/loading and coverall during application (EFSA, 2011; EU notification).

CILLS Countries

In the notification and supporting documentation, risks to operators are also reported:

Reference is made to the EFSA report (2011), which mentions that health risks for operators were accentuated because the estimated exposure to EC formulations recorded higher values (between 1435% and 5550%) than the acceptable operator exposure level (AOEL), despite the use of trailed sprayer and the use of gloves during mixing, loading and application. Without PPE, values up to 35550% of the AOEL are reported.

Contrary to USA and EU countries, the recommended use in Sahel countries was low volume application (knapsack sprayer) of the formulation diluted with water at doses between 2.5 and 3.5 l /ha on cotton. Frequency of application was once a crop-year. Recommended protection devices were protective clothing, goggles and gloves.

In the CILSS countries, people experience difficulties in finding suitable personal protective equipment. Farmers don't use appropriate personal protective equipment (Gomgnimbou et al., 2010, Ouedraogo et al., 2009, Toe et al, 2010). The protective equipment sold to farmers were essentially masks, boots and gloves. Masks are the most used (40% of farmers use them, 39% of which are dust masks against 1% are masks cartridge filters), followed by boots (28.8%), with the combination of the two are the least used used (4.5%). 12.62 % of farmers wear both masks and boots, while only 0.93% wears gloves, boots, overall, mask and glasses at the same time. Masks with filter cartridges are worn in combination with gloves, boots, coveralls and goggles in only 0.31% of cases. (Toe, 2010). This equipment is not specific to carry out treatments which require the full protection of operators (as for acetochlor based formulations).

3.5 Medical data contributing to regulatory decision

Not available.

3.6 Public exposure

Information available in sections 3.1. – 3.3.

3.7 Summary-overall risk evaluation

European Union

During the evaluation of this active substance, in particular the following concerns were identified: A potential human exposure above the acceptable daily intake has been identified. In addition, there is a potential for human exposure to the surface water metabolite t-norchloro acetochlor, the genotoxicity of which cannot be excluded. There is a high risk of groundwater contamination for several metabolites, a high risk for aquatic organisms and a high long term risk for herbivorous birds. Finally, the information available was not sufficient to conclude on the risk assessment for the groundwater contamination for metabolites t-norchloroacetochlor and t-hydroxyacetochlor (Commission Implementing Regulation (EU) 1372/2011).

CILSS Countries

The Sahelian Pesticides Committee recommended to stop the authorization of the pesticide formulations containing acetochlor because of the following reasons:

- Risks of water resources contamination from several metabolites including t-norchloro acetochlor;

The CILSS countries concluded that using acetochlor as a pesticide under these conditions resulted an unacceptable risk to human health because of drinking water contamination. Further, the following was taken into account (UNEP/FAO/RC/CRC.13/INF/8):

- Difficulties for the population to get adequate personal protection equipment;
- The fragile ecology of CILSS countries characterized by torrential rains on soils which are often poor in organic matter and thus highly subject to erosion and leaching;
- The absence of an environment management system respecting buffer strips between treated fields and water courses, the use of surface water as drinking water for man and animals;
- The use of groundwater as the only reservoir of drinking water;
- The existence of alternatives to the use of acetochlor.

4 Environmental fate and effects

4.1 Fate

4.1.1 Soil

European Union

In topsoil under aerobic conditions acetochlor exhibits low to moderate persistence forming the major soil metabolites t-oxanilic acid (max 17% applied radioactivity (AR)) and t-sulfonic acid (max 11.8% AR) which exhibited moderate to high persistence and t-sulfinylacetic acid (max 18% AR) which exhibited medium to high persistence. The minor soil metabolites s-sulfonic acid (max 9.8% AR) which exhibited moderate to medium persistence and t-norchloro acetochlor (max 3.3% AR) were also identified. Mineralisation of the phenyl radiolabel to carbon dioxide accounted only 0.3-3.1% of applied radioactivity (AR) after 96 days. The formation of unextractable residues was also a significant sink accounting for 15-41% AR after 84-90 days. Acetochlor exhibits high to medium mobility in soil, t-oxanilic acid, t-sulfinyl acetic acid and t-sulfonic acid exhibit very high to high mobility in soil and s-sulfonic acid and t-norchloro acetochlor exhibit very high mobility in soil. There was no indication that adsorption of either acetochlor or these 5 metabolites was pH dependent.

Acetochlor shows low to moderate persistence in soil, with DT50 values of 3.4 – 29 days in a laboratory setting and 7-17 days in the field. (EFSA, 2011; EU notification)

CILSS countries

When acetochlor enters the soil, it has high to moderate mobility based on a Koc range of 98.5 to 335. Little volatilisation from moist soil surface should occur based on its Henry's constants evaluation of 2.7 x 10-10 atm-cu m/mole. Acetochlor degradation is 8 to 15% in loamy sand during 48-day incubation period, which shows that biodegradation is an important environmental fate process in the soil. Persistence is moderate, DT_{50} = 2 to 3 months.

Adsorption occurs more easily in silty and clay soils rather than in soils with a moderate content of clay or organic matter. Acetochlor adsorbs little to soil particles which means an important potential of runoff and surface water contamination. Metabolism leads to the formation of toxic metabolites such as t-norchloro acetochlor. However, due to its moderate mobility, the risk of surface water contamination by runoff is moderate. This contamination concerns watercourses by runoff but also groundwater by infiltration (CILSS countries supporting documentation).

4.1.2 Water

European Union

In natural sediment water systems acetochlor exhibited moderate persistence degrading to the major metabolites t-oxanilic acid (2) (max. 13.1% AR in water) and t-norchloro acetochlor (6) (max10.4% AR in water 19.2% AR in sediment). The terminal metabolite, CO_2, was a small sink in the material balance accounting for only 1.4-2.7% AR at 100 days. Un-extracted sediment residues were the most significant sink for radioactivity representing 24-50% AR at 100 days.

The potential for groundwater exposure from the applied for intended uses above the parametric drinking water limit of 0.1 µg/L by parent acetochlor was concluded to be low, in geoclimatic situations that are represented by all 9 FOCUS groundwater scenarios. A high potential for groundwater contamination >0.1 µg/L over significant areas of the EU by the metabolites t-oxanilic acid, t-sulfinylacetic acid, t-sulfonic acid and s-sulfonic acid that have (on the basis of the available mammalian toxicology data) been concluded as relevant metabolites was identified. A data gap was identified for the stability of the metabolites t-norchloroacetochlor and t-hydroxyacetochlor in stored frozen groundwater samples. (EFSA, 2011, EU notification)

CILSS countries

Acetochlor is not expected to absorb to suspended matter and sediments if entering the soil. Acetochlor half-life in sewage sludge was set at 17.2 hours, which shows that biodegradation can be an important environmental fate process in water. Little volatilisation from moist soil surface is expected to occur based on the Henry's constants evaluation of that compound. A first order hydrolysis has been described

with half-life in water of 1386, 2310 and 2310 days at pH 4, pH 7 and 10, respectively. (CILSS supporting documentation,).

4.1.3	Air	**European Union** Vapour pressure of acetochlor (2.2×10^{-3} Pa at 20°C) indicates very slight volatility under the national scheme of the Netherlands. Therefore, losses due to volatilisation might be expected to be minimal. Calculations using the method of Atkinson for indirect photo-oxidation in the atmosphere through reaction with hydroxyl radicals resulted in an atmospheric half-life estimated at 2.3 hours. Therefore, the proportion of applied acetochlor that did volatilise would be unlikely to be subjected to long-range atmospheric transport. (EFSA, 2011, EU notification) **CILSS countries** A vapour pressure of acetochlor in the air of $1,67 \times 10^{-5}$ mmHg at 20 °C suggests that acetochlor will not exist in vapour and particle phases in the atmosphere to any significant extent. In the vapour phase, acetochlor will degrade in the atmosphere by reaction with hydroxyl radicals; air half-life for that reaction is estimated 2.6 hours. In particle phase, acetochlor will be removed from the atmosphere by wet or dry deposition process. Acetochlor may be sensitive to direct photolysis by sunlight. (CILSS notification)
4.1.4	Bioconcentration	**European Union** The risk of bioconcentration of acetochlor is considered to be low in fish (EFSA, 2011). The risk to fish-eating birds and mammals was assessed as low in the first-tier risk assessment but the trigger of 5 was not met for earthworm-eating birds and mammals and a data requirement was identified in the DAR. A refined risk assessment based on measured BCF in earthworms was presented in addendum 1 (of the DAR). The experts agreed that it is likely that the high content of sphagnum peat (10% instead of 5%) did not influence the outcome of the bioconcentration study because of the low Koc value of acetochlor. The experts suggested calculating the BCF on the basis of total radioactivity. The TER calculation with the BCF of 0.316 (based on total radioactivity) would result in TERs above the trigger (indicating no risk). (EFSA, 2011)
4.1.5	Persistence	**European Union** The water-sediment study (2 systems studied at 20°C in the laboratory) demonstrated acetochlor exhibited moderate persistence dissipating in the total systems with estimated single first order DT_{50} of 17-22 days (DT90 56-75 days). In soil, the substance showed low to moderate persistence ($DT_{50\ lab}$ = 3.4-29 d, 20°C, pF2 (-10kPa), $DT_{50\ field}$ = 7-17 d) (EFSA, 2011).
4.2	Effects on non-target organisms	
4.2.1	Terrestrial vertebrates	**European Union** **Terrestrial birds** Bobwhite quail, acetochlor, acute LD_{50} : 928 mg a.s./kg bw GF-675, acute LD_{50}: 1345 mg a.s./kg bw MON 69447, acute LD_{50}: 375 mg a.s./kg bw Mallard duck, acetochlor, short-term LC_{50}: 1057 mg a.s./kg bw/day Mallard duck, acetochlor, long-term NOEC: 5.5 mg a.s./kg bw/day (EFSA, 2011).
4.2.2	Aquatic species	**European Union** **Freshwater Species** **Aquatic invertebrates** *Daphnia magna* Acetochlor, 48 h (static), mortality, EC_{50}: 8.6 mg/l Acetochlor, 21 d (static), reproduction, NOEC: 0.0221 mg/l WF 2061, 48 h (static), EC_{50}: 7.4 mg/l GF-675, 48 h (static), mortality, EC_{50} >6.4 mg/l t-oxanilic acid, 48 h (static), EC_{50} >120 mg/l, NOEC = 120 mg/l

t-sulfinylacetic acid, 48 h (static), EC_{50} >120 mg/l, NOEC = 120 mg/l
t-sulfonic acid, 48 h (static), EC_{50} >120 mg/l, NOEC = 120 mg/l
t-norchloroacetochlor, 48 h (static), EC_{50}: 170 mg/l, NOEC = 100 mg/l
(EFSA, 2011)

Algae
P. subcapitata
Acetochlor, 72 h, Biomass EbC_{50} : 0.00031 mg/l, growth rate ErC_{50}: 0.00052 mg/l
Acetochlor, 120 h (static), growth rate ErC_{50}: 0.00019 mg/l GF-675, 72 h (static), Biomass EbC_{50}: 0.00077 mg/l, growth rate ErC_{50}: 0.0010 mg/l MON 69447, 72 h (static), Biomass EbCsev 0.00071 mg/l, growth rate ErC_{50}: 0.00155 mg/l t-oxanilic acid, 72 h (static), EbC_{50}: 44 mg/l, ErC_{50}: 42 mg/l, NOEr/bC: 32 mg/l,
sulfinylacetic, 72 h (static), EbC_{50}: 57 mg/l, ErC_{50}: 68 mg/l NOEbC: 32 mg/l, NOErC: 56 mg/l t-sulfonic acid, 72 hours (static), EbC_{50}: 8.1 mg/l, ErC_{50}: 17 mg/l, NOEb/rC: 3.2 mg/l t-norchloro acetochlor, 72 hours (static), EbC_{50} : 0.34 mg/l, ErC_{50} : 0.49 mg/l, NOEbC: 0.12 mg/l, NOErC: 0.24 mg/l s- sulfonic acid, 72 hours (static), EbC_{50} and ErC_{50} and NOEbC all >124 mg/l (EFSA, 2011)

Aquatic plants
Lemna gibba
Acetochlor, 7 d EC_{50} (frond no): 0.0027 mg/l
MON 69447, 7 d EC_{50} (frond no): 0.00257 mg/l
GF-675, 7 d EC_{50} (frond no) > 0.00054mg/l t-oxanilic acid, 7 days static, EC_{50} (frond n°) >123 mg/l, ErC_{50} >123 mg/l, NOEC (both): 123 mg/l
t-sulfinylacetic acid, 7 days static, EC_{50} (frond n°) >112 mg/l, ErC_{50} >112 mg/l, NOEC (both): 112mg/l t-sulfonic acid, 7 days static, EC_{50} (frond n°) > 140 mg/l, ErC_{50} > 140 mg/l, NOEC > 140 mg/l
s-sulfonic, 7 days static, EC_{50} (frond n°) > 150 mg/l, ErC_{50} > 150 mg/l, NOEC (both) > 150 mg/l
Norchloroacetochlor, 7 days static, EC_{50} (frond n°): 19 mg/l, ErC_{50}: 49 mg/l, NOEC (both): 4.8 mg/l (EFSA, 2011)

Fish
Oncorhynchus mykiss, acetochlor, 96h (static), mortality EC_{50}: 0.36 mg/l
Oncorhynchus mykiss, 60 day (flow-through), growth NOEC: 0.13 mg/l
Bluegill sunfish, GF 675, 96 h (static) mortality EC_{50}: 1.07 a.s. mg/l
Oncorhynchus mykiss
MON 69447, 96 h (flow-through), mortality EC_{50}: 0.547 a.s. mg/l
t-oxanilic acid, 96 h (static), mortality LC_{50} >93 mg/l
t-sulfinylacetic acid, 96 h (static), mortality LC_{50} >120 mg/l
t-sulfonic acid, 96 h (static), mortality LC_{50} >180 mg/l
t-norchloro acetochlor acid, 96 h (static), mortality LC_{50}: 42 mg/l (EFSA, 2011)

4.2.3 Honeybees and other arthropods

European Union
Honey Bee
Acetochlor, acute LD_{50} oral >100 a.s. µg/bee, contact > 200 µg/bee
Preparation WF-2061, MON 69447 and the metabolites, t-oxanilic acid, t-sulfinylacetic acid, t-sulfonic acid, s-sulfonic acid, acute LD_{50} oral and contact all >86.7 µg/bee, (EFSA, 2011)

Other Arthropod Species
Laboratory tests
Mortality with GF-675
Typhlodromus pyri, LR_{50}: 831 g a.s/ha
Aphidius rhopalosiphi, LR_{50}:156 g a.s/ha (EFSA, 2011)
P. *cupreus*, $LR^{5}9_{50}$ M = 0% at 2000 g a.s./ha
Chrysoperla carnea, LR_{50} M = 0% at 2000 g a.s./ha
(EFSA, 2011)

4.2.4	**Earthworms**	**European Union** **Earthworm** *Eisenia foetida* Acetochlor, acute 14-days LC_{50}: 105.5 mg a.s./kg dw soil MON69447, acute 14-days LC_{50}: 221 mg a.s./kg dw soil Oxanilic acid, t-sulfinylacetic acid, t-sulfonic acid, s-sulfonic acid; acute 14-days LC_{50} >500 mg a.s./kg dw soil Oxanilic acid, chronic NOEC: 3.39 mg a.s./kg dw soil t-sulfinylacetic acid, NOEC: 3.44 mg a.s./kg dw soil t-sulfonic acid, NOEC: 3.71 mg a.s./kg dw soil s-sulfonic acid, NOEC: 10.5 mg a.s./kg dw soil (EFSA, 2011)
4.2.5	**Soil microorganisms**	**European Union** The effects of the lead acetochlor based formulations were tested on soil microbial respiration and nitrogen transformation. The risk to soil non-target micro-organisms from acetochlor is considered to be low for the representative uses evaluated. (EFSA, 2011).
4.2.6	**Terrestrial plants**	**European Union** Studies with technical acetochlor and different formulations on the influence on seedling emergence and plant vigour are available. The risk assessment presented in the DAR was based on species sensitivity distribution on endpoints for 21 plant species. Overall it is concluded that a high risk to non-target plants cannot be excluded and risk mitigation measures comparable to a no spray buffer zone (in-field) of 5 m is required. (EFSA, 2011).

5 Environmental Exposure/Risk Evaluation

5.1	**Terrestrial vertebrates**	**European Union** The short-term toxicity-exposure ratio (TER) for birds and the acute and long-term TERs for mammals were above the trigger of 10 and 5 in the first-tier risk assessment. A residue decline study was submitted. The acute risk to herbivorous birds was sufficiently addressed on the basis of measured residues. However, the suggested 'proportion of different food types in the diet' (PD) and 'proportion of diet obtained in treated area' (PT) values to refine the long-term risk to herbivorous birds were assessed and considered as not supported by the submitted data. The refined risk assessment for insectivorous birds based on crested lark (*Galerida cristata*) was agreed by the meeting. The risk from consumption of contaminated water was assessed as low for mammals. It was agreed in the expert meeting, that the risk to mammals is low. However, a high acute risk was indicated for birds for post-emergence applications where accumulation of water in leaf axils of maize plants can occur. The risk from secondary poisoning of fish-eating birds and mammals was assessed as low in the first tier but further refinement was required for earthworm-eating birds and mammals. The risk was sufficiently addressed using data from a bioconcentration study with earthworms. The risk from soil metabolites was considered to be low because their log Pow is <3 suggesting a low potential of bioconcentration and bioaccumulation in the food chain. Endpoints from acute toxicity studies with rats were available for the major plant metabolite N-oxamic acid (68) and for metabolite 3 (t-sulfinylacetic acid). No information on the toxicity to birds was available. In the risk assessment it was assumed that the metabolites have a similar toxicity to birds as the parent. The acute and long-term TERs for birds and mammals were above the triggers of 10 and 5. However some uncertainty remains because of the high proportion of unidentified residues in the residue trials (EFSA, 2011). **CILSS Countries** In the supporting documentation, high acute risk to birds from uptake of contaminated drinking water was indicated for the post emergence applications and high long term risk for herbivorous birds was mentioned.

5.2	**Aquatic species**	**European Union** Acetochlor is very toxic to all groups of aquatic organisms and a high risk was indicated in the risk assessment with the FOCUS model step3 PECsw. A risk refinement based on endpoints from a static mesocosm and from a mesocosm with a pulsed exposure regime was used to refine the risk in lentic and lotic water bodies. The experts agreed that the 'no observed adverse effect concentration' (NOAEC) of 0.2 µg acetochlor/L for lentic water bodies and the NOAEC of 2 µg acetochlor/L for lotic water bodies should be used in the risk assessment together with an assessment factor of 2-3. No FOCUS model step 4 scenario resulted in a TER exceeding the trigger of 2 even when no-spray buffer zones of 20m and vegetated filter strips of 20m were applied to mitigate the risk. Overall it is concluded that the risk to aquatic organisms from exposure to acetochlor is high for the representative uses evaluated. The risk from metabolites in water and sediment was assessed as low. The bioconcentration potential of acetochlor was assessed as low (EFSA, 2011). **CILSS Countries** In the supporting documentation, it is mentioned that acetochlor is very toxic to all groups of aquatic organisms and there is a high risk to aquatic organisms.
5.3	**Honey bees**	**European Union** The risk to bees, soil macro-organisms, organic matter breakdown and biological methods of sewage treatment was assessed as low for the representative uses of acetochlor (EFSA, 2011).
5.4	**Earthworms**	**European Union** The acute risk of acetochlor to earthworms was assessed as low. No long-term risk assessment is triggered because the representative uses cover only one application per year and the field DT90 is <100 days. The acute and long-term risk from soil metabolites to earthworms was assessed as low (EFSA, 2011).
5.5	**Soil microorganisms**	The risk to soil-micro-organisms was assessed as low for the representative uses of acetochlor (EFSA, 2011).
5.6	**Summary – overall risk evaluation**	**European Union** During the evaluation of this active substance, in particular the following concerns were identified: There is a high risk of groundwater contamination for several metabolites, a high risk for aquatic organisms and a high long term risk for herbivorous birds. **CILSS Countries** The Sahelian Pesticides Committee recommended stopping the authorization of the pesticide formulations containing acetochlor because of the following reasons: • Risks of water resources contamination from several metabolites including t-norchloro acetochlor; • High risk to aquatic organisms and long term risks to herbivorous birds Further, the following was taken into account (UNEP/FAO/RC/CRC.13/INF/8): • The fragile ecology of CILSS countries characterized by torrential rains on soils which are often poor in organic matter and thus highly subject to erosion and leaching; • The absence of an environment management system respecting buffer strips between treated fields and water courses, the use of surface water as drinking water for man and animals; • The existence of alternatives to the use of acetochlor.

Annex 2 – Details on final regulatory actions reported

Country Name: European Union

1	**Effective date(s) of entry into force of actions**	23 June 2013
	Reference to the regulatory document	Commission Implementing Regulation (EU) No 1372/2011 of 21 December 2011 concerning the non-approval of the active substance acetochlor, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending Commission Decision 2008/934/EC (Official Journal of the European Union L 341, 22.12.2011, p. 45-46). https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32011R1372
2	**Succinct details of the final regulatory action(s)**	It is prohibited to place on the market or use plant protection products containing acetochlor in the European Union. Acetochlor is not approved for placing on the market pursuant to Regulation (EC) No. 1107/2009 concerning the placing of plant protection products on the market (which replaces Directive 91/414/EEC). All authorisations for plant protection products containing acetochlor had to be withdrawn by the Member States by 23 June 2012 and all uses of plant protection products containing acetochlor are prohibited as of 23 June 2013 at the latest.
3	**Reasons for action**	Reduction of risk from the use of plant protection products containing acetochlor to human health and the environment.
4	**Basis for inclusion into Annex III**	The final regulatory action was taken to protect human health and the environment. The regulatory action was based on a risk evaluation taking into account the prevailing conditions in the EU.
4.1	**Risk evaluation**	During the evaluation of this active substance, in particular the following concerns were identified: A potential human exposure above the acceptable daily intake has been identified. In addition, there is a potential for human exposure to the surface water metabolite t-norchloro acetochlor, the genotoxicity of which cannot be excluded. There is a high risk of groundwater contamination for several metabolites, a high risk for aquatic organisms and a high long term risk for herbivorous birds. Finally, the information available was not sufficient to conclude on the risk assessment for the groundwater contamination for metabolites t-norchloro acetochlor and t-hydroxyacetochlor (Commission Implementing Regulation (EU) 1372/2011). **Safety Values:** Acceptable Daily Intake (ADI): 0.0036 mg/kg bw/day (78-week mouse study and Safety Factor of 300 (3x100); the additional factor of 3 was used because of the use of the LOAEL). Acceptable Operator Exposure Level (AOEL): 0.02 mg/kg bw/day (1-year dog study with Safety Factor of 100). Acute Reference Dose (ARfD): 1.5 mg/kg bw/day (acute neurotoxicity in rat and safety factor of 100). (EU and CILSS notifications) (EFSA, 2011)
4.2	**Criteria used**	Risk to human health and the environment.
	Relevance to other States and Region	The use of pesticides containing acetochlor may cause similar problems to health and the environment in other countries (EU notification).
5	**Alternatives**	The notifying Party did not provide information on alternatives for the use of acetochlor.
6	**Waste management**	The notifying Party did not provide information on waste management of acetochlor.
7	**Other**	None.

Country Name: Burkina Faso, Cabo Verde, Chad, the Gambia, Guinea-Bissau, Mali, Mauritania, the Niger, Senegal and Togo (CILSS countries)

1	**Effective date(s) of entry into force of actions**	20 March 2017
	Reference to the regulatory document	Decision N 002/CM/2017 of CILSS coordinating Ministry
2	**Succinct details of the final regulatory action(s)**	On recommendation of the Sahelian Pesticide Committee (CSP), Decision N°002/MC/2017 to ban all products containing acetochlor was signed on 20 March 2017 by CILSS coordinating Ministry. The final regulatory action entered into force on 20 March 2017. The use of all pesticides containing acetochlor has been banned due to its potential for water contamination. The import, manufacture for domestic use, distribution and sale are also banned.
3	**Reasons for action**	Reduction of risk from the use of plant protection products containing acetochlor to human health and the environment.
4	**Basis for inclusion into Annex III**	The final regulatory action was taken to protect human health and the environment. The regulatory action was based on a risk evaluation taking into account the prevailing conditions in the CILSS countries.
4.1	**Risk evaluation**	The Sahelian Pesticides Committee recommended stopping the authorization of the pesticide formulations containing acetochlor because of the following reasons: • Risks of water resources contamination from several metabolites including t-norchloro acetochlor; • Unacceptable risk to human health because of drinking water contamination • High risk to aquatic organisms and long term risks to herbivorous birds. Further, the following was taken into account (UNEP/FAO/RC/CRC.13/INF/8): • Difficulties for the population to get adequate personal protection equipment; • The fragile ecology of CILSS countries characterized by torrential rains on soils which are often poor in organic matter and thus highly subject to erosion and leaching; • The absence of an environment management system respecting buffer strips between treated fields and water courses, the use of surface water as drinking water for man and animals; • The use of groundwater as the only reservoir of drinking water; • The existence of alternatives to the use of acetochlor.
4.2	**Criteria used**	Risk to human health and the environment.
	Relevance to other States and Region	The use of pesticides containing acetochlor may cause similar problems to health and the environment in other countries (CILSS countries notification).
5	**Alternatives**	Alternatives to the use of acetochlor based formulations do exist. As an alternative, selective pesticide formulations are registered and authorised for sale in CILSS countries. Several selective pesticide formulations can be found in the global list of pesticides registered by the Sahelian Pesticide Committee (CSP) for maize and for cotton (CSP, 2016, see website: www.insah.org) (CILSS countries notification).
6	**Waste management**	The notifying Party did not provide information on waste management of acetochlor.
7	**Other**	None.

Annex 3 – Addresses of designated national authorities

CILSS Countries: Burkina Faso, Cabo Verde, Chad, the Gambia, Guinea-Bissau, Mali, Mauritania, the Niger, Senegal and Togo

Burkina Faso Ministère de l'Agriculture et des Aménagements Hydrauliques Direction Générale des Productions Végétales Direction de la Protection des Végétaux et du Conditionnement DPVC 01 BP: 5362 Ouagadougou 01 OUATTARA Moussa Directeur de la Protection de Végétaux et du Conditionnement	Phone: +226 25361915 / +226 71353315 E-mail: outtmouss@yahoo.fr / dpvcagriculture@yahoo.fr
Cabo Verde Ministère de l'Agriculture et de l'Environnement (MAA) Direction Générale de l'Agriculture, Sylviculture et Elevage (DGASP) BP 278 Praia Ilha de Santiago Cabo Verde Celestino Gomes Mendes Tavares AND Pesticides	Phone: +238 5160089 E-mail: Celestino.Tavares@maa.gov.cv
Chad Ministère en charge de l'Agriculture Dicrection de la protection des végétaux et du conditionnement BP 1551 N'Djamena Chad Moussa Abderaman Abdoulaye Directeur AND/Pesticide/Chad	Phone: +235 66325252 E-mail: Charafa2009@gmail.com
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Guinea-Bissau Ministère de l'Agriculture, Foret et Elevage / Direction de la Protection des Végétaux Granja de Pessubé. BP : 844 – Bissau Eng. Pedro Correia Landim AND Convention de Rotterdam Responsable de la législation et contrôle des pesticides	Phone: +245955996830 E-mail: pedrocorreialandim@yahoo.com.br
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Togo Ministry of Agriculture BP 5054 Nouakchott-Mauritanie Sow Moussa Mamadou Technical advisor responsible for the agricultural sector and plant protection	Phone +222 46463939 Fax +222 45257475 E-mail sowmoussa635@yahoo.fr

European Union	
European Commission DG Environment BU-9, 06/164 B-1049 Brussels Belgium Dr. Juergen Helbig Policy Officer	**Phone** +32 2 298 8521 **Fax** +32 2 296 7617 **E-mail** Juergen.Helbig@ec.europa.eu

Annex 4 – References

Regulatory actions

European Union

Commission Implementing Regulation (EU) No 1372/2011 of 21 December 2011 concerning the non-approval of the active substance acetochlor, in accordance with Regulation (EC) No 1107/2009 of the European Parliament and of the Council concerning the placing of plant protection products on the market, and amending Commission Decision 2008/934/EC (Official Journal of the European Union L 341, 22.12.2011, p. 45-46). http://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32011R0341

CILSS countries

Decision N°002/CM/2017 of CILSS coordinating Ministry

Supporting Documentation

European Union

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WHO and FAO

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UNITED NATIONS

UNEP

Food and Agriculture Organization of the United Nations

RC

UNEP/FAO/RC/CRC.14/4

Distr.: General
25 May 2018

Original: English

Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade

Chemical Review Committee
Fourteenth meeting
Rome, 11–14 September 2018
Item 4 (a) (ii) of the provisional agenda*

Technical work: consideration of draft decision guidance documents: hexabromocyclododecane

Draft decision guidance document for hexabromocyclododecane

Note by the Secretariat

I. Introduction

1. At its thirteenth meeting, the Chemical Review Committee reviewed notifications of final regulatory action for hexabromocyclododecane submitted by Japan and Norway, together with the supporting documentation referenced therein, and concluded that the notifications met all the criteria of Annex II to the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade.

2. In its decision CRC-13/2, the Committee recommended that the Conference of the Parties list hexabromocyclododecane in Annex III to the Convention as an industrial chemical. In the same decision, the Committee adopted a rationale for its conclusions, decided to prepare a draft decision guidance document for hexabromocyclododecane and also decided on the composition of the intersessional drafting group to prepare the document. A detailed workplan for the development of the draft decision guidance document was prepared by the Committee in line with the process adopted by the Conference of the Parties by decision RC-2/2 and amended by decisions RC-6/3 and RC-7/3. The recommendation, rationale and workplan were annexed to the report of the Committee on the work of its thirteenth meeting (UNEP/FAO/RC/CRC.13/19, annexes I and III).

3. The material available to the intersessional drafting group included a summary of the outcome of the thirteenth meeting of the Committee, a copy of the working paper on the preparation of internal proposals and decision guidance documents for banned and severely restricted chemicals and the notifications of final regulatory action, and associated supporting documentation available to the Committee at its thirteenth meeting.

4. In accordance with the agreed workplan, Mr. Jeffery R. Goodman (Canada), the chair of the intersessional drafting group, and Mr. Arsonina Bera (Madagascar), the vice-chair, prepared an internal proposal based on the notifications and the supporting documentation. That internal proposal was circulated to the members of the drafting group for comment on 18 December 2017. It was amended in the light of the comments received and was circulated on 23 February 2018 to all Committee members and to the observers who had attended the thirteenth meeting. Responses were received from Committee members and observers and taken into consideration in the preparation of the draft decision guidance document.

* UNEP/FAO/RC/CRC.14/1

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5. The draft decision guidance document and a compilation of the comments received were circulated to the members of the drafting group on 30 April 2018.

6. The text of the draft decision guidance document, as submitted by the drafting group, is set out in the annex to the present note. It has not been formally edited. A tabular summary of the comments received, including information on how they were addressed, is set out in the annex to the note by the Secretariat on the matter (UNEP/FAO/RC/CRC.14/INF/7).

II. Proposed action

7. The Committee may wish to finalize the draft decision guidance document and to forward it, together with its recommendation to list hexabromocyclododecane in Annex III to the Convention as an industrial chemical, for consideration by the Conference of the Parties at its ninth meeting.

Annex

Rotterdam Convention

Operation of the prior informed consent procedure for banned or severely restricted chemicals

Draft Decision Guidance Document

Hexabromocyclododecane

Secretariat of the Rotterdam Convention
on the Prior Informed Consent Procedure
for Certain Hazardous Chemicals and Pesticides
in International Trade

Food and Agriculture Organization of the United Nations

UNEP

Introduction

The objective of the Rotterdam Convention is to promote shared responsibility and cooperative efforts among Parties in the international trade of certain hazardous chemicals in order to protect human health and the environment from potential harm and to contribute to their environmentally sound use, by facilitating information exchange about their characteristics, by providing for a national decision-making process on their import and export and by disseminating these decisions to Parties. The Secretariat of the Convention is provided jointly by the United Nations Environment Programme (UNEP) and the Food and Agriculture Organization of the United Nations (FAO).

Candidate chemicals[1] for inclusion in the prior informed consent (PIC) procedure under the Rotterdam Convention include those that have been banned or severely restricted by national regulatory actions in two or more Parties[2] in two different regions. Inclusion of a chemical in the PIC procedure is based on regulatory actions taken by Parties that have addressed the risks associated with the chemical by banning or severely restricting it. Other ways might be available to control or reduce such risks. Inclusion does not, however, imply that all Parties to the Convention have banned or severely restricted the chemical. For each chemical included in Annex III of the Rotterdam Convention and subject to the PIC procedure, Parties are requested to make an informed decision whether they consent or not to the future import of the chemical.

At its [...] meeting, held in [...] on [...], the Conference of the Parties agreed to list hexabromocyclododecane in Annex III of the Convention and adopted the decision-guidance document with the effect that this chemical became subject to the PIC procedure.

The present decision-guidance document was communicated to designated national authorities on [...], in accordance with Articles 7 and 10 of the Rotterdam Convention.

Purpose of the decision guidance document

For each chemical included in Annex III of the Rotterdam Convention, a decision-guidance document has been approved by the Conference of the Parties. Decision-guidance documents are sent to all Parties with a request that they make a decision regarding future import of the chemical.

Decision-guidance documents are prepared by the Chemical Review Committee. The Committee is a group of government-designated experts established in line with Article 18 of the Convention, which evaluates candidate chemicals for possible inclusion in Annex III of the Convention. Decision-guidance documents reflect the information provided by two or more Parties in support of their national regulatory actions to ban or severely restrict the chemical. They are not intended as the only source of information on a chemical nor are they updated or revised following their adoption by the Conference of the Parties.

There may be additional Parties that have taken regulatory actions to ban or severely restrict the chemical and others that have not banned or severely restricted it. Risk evaluations or information on alternative risk mitigation measures submitted by such Parties may be found on the Rotterdam Convention website (www.pic.int).

Under Article 14 of the Convention, Parties can exchange scientific, technical, economic and legal information concerning the chemicals under the scope of the Convention including toxicological, ecotoxicological and safety information. This information may be provided directly to other Parties or through the Secretariat. Information provided to the Secretariat will be posted on the Rotterdam Convention website.

Information on the chemical may also be available from other sources.

Disclaimer

The use of trade names in the present document is primarily intended to facilitate the correct identification of the chemical. It is not intended to imply any approval or disapproval of any particular company. As it is not possible to include all trade names presently in use, only a number of commonly used and published trade names have been included in the document.

While the information provided is believed to be accurate according to data available at the time of preparation of the present decision-guidance document, FAO and UNEP disclaim any responsibility for omissions or any consequences that may arise there from. Neither FAO nor UNEP shall be liable for any injury, loss, damage or prejudice of any kind that may be suffered as a result of importing or prohibiting the import of this chemical.

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[1] According to the Convention, the term "chemical" means a substance, whether by itself or in a mixture or preparation and whether manufactured or obtained from nature, but does not include any living organism. It consists of the following categories: pesticide (including severely hazardous pesticide formulations) and industrial.

[2] According to the Convention, the term "Party" means a State or regional economic integration organization that has consented to be bound by the Convention and for which the Convention is in force.

The designations employed and the presentation of material in this publication do not imply the expression of any opinion whatsoever on the part of FAO or UNEP concerning the legal status of any country, territory, city or area or of its authorities or concerning the delimitation of its frontiers or boundaries.

Standard core set of abbreviations[3]

STANDARD CORE SET OF ABBREVIATIONS	
<	less than
≤	less than or equal to
>	greater than
≥	greater than or equal to
µg	Microgram
µm	micrometre
BAF	Bioaccumulation factor
BCF	Bioconcentration factor
bw	body weight
BMDL	Benchmark Does lower confidence bound
BMR	Benchmark Response
°C	degree Celsius (centigrade)
CAS	Chemical Abstracts Service
cm	centimetre
DNA	deoxyribose nucleic acid
DT_{50}	dissipation time 50%
DfE	Design for the Environment (US EPA program)
dw	dry weight
EC	European Community
EC_{50}	median effective concentration
ECHA	European Chemicals Agency
EEC	European Economic Community
EPS	Expanded polystyrene
EU	European Union
FAO	Food and Agriculture Organization of the United Nations
g	gram
h	hour
HBCDD	Hexabromocyclododecane
IARC	International Agency for Research on Cancer

[3] *This core list should serve as the basis for DGDs for industrial chemicals, pesticides and severely hazardous pesticide formulations. It should be augmented by abbreviations used in the individual DGDs relevant to the chemical(s) in question.*

Definitions and spelling should, as far as practicable, follow the IUPAC glossary of terms in toxicology and the IUPAC glossary of terms relating to pesticides in their current editions.

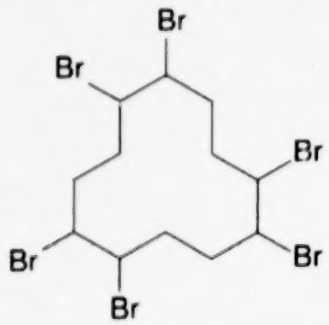
As a general rule it is preferable that acronyms used only once in the text be spelled out rather than included in the list of abbreviations.

STANDARD CORE SET OF ABBREVIATIONS	
IPCS	International Programme on Chemical Safety
IUPAC	International Union of Pure and Applied Chemistry
k	kilo- (x 1000)
kg	kilogram
L	litre
LC_{50}	median lethal concentration
LD_{50}	median lethal dose
LOAEL	lowest-observed-adverse-effect level
lw	liquid weight
m	metre
mg	milligram
ml	millilitre
MW	Molecular Weight
NES	no effects at saturation
ng	nanogram
NOAEL	no-observed-adverse-effect level
NOEC	no-observed-effect concentration
NOHSC	National Occupational Health and Safety Commission
OECD	Organisation for Economic Co-operation and Development
POPRC	Persistent Organic Pollutants Review Committee of the Stockholm Convention
PPE	personal protective equipment
ppm	parts per million (used only with reference to the concentration of a pesticide in an experimental diet. In all other contexts the terms mg/kg or mg/L are used).
TH	Thyroid hormone
TSH	Thyroid-stimulating hormone
UNEP	United Nations Environment Programme
US EPA	United States Environmental Protection Agency
w/w	weight for weight
WHO	World Health Organization
wt	weight
wwt	Wet weight
XPS	Extruded polystyrene

Decision guidance document for a banned or severely restricted chemical

HEXABROMOCYCLODODECANE **Published:**

1. Identification and uses (see Annex 1 for further details)

Common name	Hexabromocyclododecane (HBCDD)
Chemical name and other names or synonyms	Hexabromocyclododecane 1,2,5,6,9,10-hexabromocyclododecane
Molecular formula	$C_{12}H_{18}Br_6$
Chemical structure	
CAS-No.(s)	25637-99-4: Hexabromocyclododecane Commercial substance (does not specify the bromine positions) 3194-55-6: 1,2,5,6,9,10- Hexabromocyclododecane 134237-50-6: α- Hexabromocyclododecane stereoisomer 134237-51-7: β- Hexabromocyclododecane stereoisomer 134237-52-8: γ- Hexabromocyclododecane stereoisomer
Harmonized System Customs Code	2903.89
Other numbers	EC Number 247-148-4, EC Number 221-695-9
Category	Industrial
Regulated category	Industrial chemical
Use(s) in regulated category	**Japan:** Flame retardant **Norway:** Hexabromocyclododecane has been used to produce flame retarded expanded polystyrene (EPS) and extruded polystyrene (XPS) for onward use in building applications abroad.
Trade names	Cyclododecane, hexabromo; HBCD; Bromkal 73-6CD; Nikkafainon CG 1; Pyroguard F 800; Pyroguard SR 103; Pyroguard SR 103A; Pyrovatex 3887; Great Lakes CD-75P™; Great Lakes CD-75; Great Lakes CD75XF; Great Lakes CD75PC (compacted); Dead Sea Bromine Group Ground FR 1206 I-LM; Dead Sea Bromine Group Standard FR 1206 I-LM; Dead Sea Bromine Group Compacted FR 1206 I-CM. (UNEP/FAO/RC/CRC.13/8 section 1.3 of the Norwegian notification – also POPRC Risk Profile section 1.1) *This is an indicative list. It is not intended to be exhaustive.*
Formulation types	Not relevant.

Uses in other categories	**Japan and Norway:** No reported use as a pesticide.
Basic manufacturers	BASF Corp. Albemarle Corp. Dow Chemical Co. Source: TOXNET (https://toxnet.nlm.nih.gov/cgi-bin/sis/search2/f?./temp/~jrwyMs:1) *This is an indicative list of current and former manufacturers. It is not intended to be exhaustive.*

2. Reasons for inclusion in the PIC procedure

Hexabromocyclododecane is included in the PIC procedure as an industrial chemical. It is listed on the basis of final regulatory actions notified by Japan and Norway that ban and severely restrict, respectively, its use as an industrial chemical.

No final regulatory actions relating to pesticidal uses of hexabromocyclododecane have been notified.

2.1 Final regulatory action (see Annex 2 for further details)

Japan:

This chemical is designated as Class I Specified Chemical Substances. It is prohibited to manufacture, import or use this chemical substance. (UNEP/FAO/RC/CRC.13/8 Sections 2 and 2.2.1 of the Japanese notification).

Reason: Human health

Norway:

Regulations to restrict production, import, export and sale of consumer products that contain hexabromocyclododecane exceeding certain limit values.

Hexabromocyclododecane is regulated by Chapter 4 of the Regulation related to restrictions on the manufacture, import and placing on the market of chemicals and other products hazardous to human health and the environment (Product Regulation) act no. 922 of June 2004. This is the Norwegian implementation of Regulation (EC) No 850/2004 of the European Parliament and of the Council on persistent organic pollutants and the implementation of the amendment to its Annex I, Commission Regulation (EU) 2016/293 of 1 March 2016. (UNEP/FAO/RC/CRC.13/8 sections 2, 2.2.1 and 2.2.2 of the Norwegian notification).

Reason: Human health and the environment

2.2 Risk evaluation (see Annex 1 for further details)

Japan:

The notification from Japan indicates that the regulatory action was based on a risk or hazard evaluation, which is provided with a focussed summary in English, and also includes the Risk Profile document for hexabromocyclododecane as prepared by the Persistent Organic Pollutants Review Committee (POPRC) of the Stockholm Convention.

When a substance is listed in the Stockholm Convention, and when it is on the market in Japan, the Japanese Government conducts a risk evaluation on the substance and its potential risks to inform the regulatory measures. This internal risk evaluation, in combination with the Risk Profile document for hexabromocyclododecane were supplied as supporting information by Japan in document UNEP/FAO/RC/CRC.13/INF/17/Rev.2. A brief English summary of that risk evaluation was provided along with the table of contents of the risk evaluation.

The internal risk evaluation was based on the monitoring data from fiscal year 2009 to fiscal year 2012 and revealed a number of sites with a high ecological risk, while there were no sites with any human health risk. The risk evaluation included a hazard assessment, an exposure assessment and risk estimation based on monitoring data, and an exposure assessment and risk estimation based on environmental releases estimated from manufacture data.

The POPRC Risk Profile document cites a Japanese study which found hexabromocyclododecane levels in human milk appearing to mirror the market consumption of hexabromocyclododecane. In mothers' milk from Japanese women (age 25–29) hexabromocyclododecane levels were below the detection limit in all samples collected during the 10-year period from 1973-1983, but then increased from 1988 onwards.

The POPRC Risk Profile document states the developmental and neurotoxic potential of hexabromocyclododecane observed in animal studies give cause for concern when considering risks to human health, particularly for unborn babies and young children. This concern, along with the human milk monitoring study and results of other studies in the Risk Profile document on cord serum, suggests some risk to unborn babies and young children in Japan.

Despite the absence of a quantitative link between the risks and the exposure levels provided, the risk is relevant given the observed bioaccumulation and biomagnification of hexabromocyclododecane.

Norway:

The notification from Norway indicates that the regulatory action was based on a risk or hazard evaluation and that it was relevant to both human health and the environment. The notification specifically cites the European Union risk assessment for hexabromocyclododecane. The notification from Norway provides a summary of evidence of exposure to consumers in Norway, its detection in the environment (including remote areas of the arctic), biota, fish, moss, yolk sac of newly hatched chicks. Some temporal trends are noted.

Hazard endpoints are provided in the supporting information from Norway, originating from the United States Environmental Protection Agency 2014 report, *Flame Retardant Alternatives for Hexabromocyclododecane (HBCD)*. High or very high hazards are noted for developmental effects, acute aquatic toxicity, and chronic aquatic toxicity. Hexabromocyclododecane is highly persistent and bioaccumulates.

3. Protective measures that have been applied concerning the chemical

3.1 Regulatory measures to reduce exposure

Japan: The regulatory action notified by Japan bans the manufacture, import and use of hexabromocyclododecane. There are no uses exempted from the ban. The regulatory action entered into force 1 May 2014. (UNEP/FAO/RC/CRC.13/8 sections 2.2 and 2.3 of the Japanese notification)

Norway: The regulatory action notified by Norway severely restricts production, import, export and sale of consumer products that contain hexabromocyclododecane exceeding certain limit values.

It is prohibited to manufacture, import, export, place on the market and use substances that contain 0.01 per cent by weight or more of hexabromocyclododecane (CAS number 25637-99-4, 3194-55-6, 134237-50-6, 134237-51-7, 134237-52-8).

It is prohibited to manufacture, import, export and make available on the market products or flame retarded parts of products that contain 0.01 per cent by weight or more of hexabromocyclododecane (CAS number 25637-99-4, 3194-55-6, 134237-50-6, 134237-51 -7, 134237-52-8).

The use of hexabromocyclododecane, whether on its own or in preparations, in the production of expanded polystyrene articles, and the production and placing on the market of hexabromocyclododecane for such use, shall be allowed provided that such use has been authorised in accordance with Title VII of Regulation (EC) No 1907/2006 of the European Parliament and of the Council, or is the subject of an application for authorisation submitted by 21 February 2014 where a decision on that application has yet to be taken.

The placing on the market and use of hexabromocyclododecane, whether on its own or in preparations, in accordance with this paragraph shall only be allowed until 26 November 2019 or, if earlier, the date of expiry of the review period specified in an authorisation decision or the date of withdrawal of that authorisation pursuant to Title VII of Regulation (EC) No 1907/2006.

(UNEP/FAO/RC/CRC.13/8 sections 2.2 and 2.3 of the Norwegian notification)

3.2 Other measures to reduce exposure

OSPAR Convention

Hexabromocyclododecane is included as part of the brominated flame retardants group in the List of Substances for Priority Action of The Convention for the Protection of the Marine Environment of the North-East Atlantic (the OSPAR Convention). The OSPAR Convention is made up of representatives of the Governments of 15 Contracting Parties and the European Union.

(UNEP/FAO/RC/CRC.13/INF/17/Rev.2 section 1.4 of the POPRC Risk Profile)

Stockholm Convention on Persistent Organic Pollutants

Hexabromocyclododecane is included in Annex A (elimination) of the Stockholm Convention on Persistent Organic Pollutants (decision SC-6/13). Specific exemptions exist for production and use of hexabromocyclododecane in expanded polystyrene and extruded polystyrene in buildings. Parties to the Stockholm Convention who register for the production and/or use exemption also agree, pursuant to Article 4, to take necessary measures to ensure that expanded polystyrene and extruded polystyrene containing

hexabromocyclododecane can be easily identified by labelling or other means throughout its life cycle when allowing the production and use of hexabromocyclododecane for expanded polystyrene and extruded polystyrene in buildings.

(Decision SC-6/13: Listing of hexabromocyclododecane. http://chm.pops.int/Portals/0/download.aspx?d=UNEP-POPS-COP.6-SC-6-13.English.pdf)

3.3 Alternatives

It is essential that before a country considers substituting alternatives, it ensures that the use is relevant to its national needs, and the anticipated local conditions of use. The hazards of the substitute materials and the controls needed for safe use should also be evaluated.

Japan:

No information on alternatives to hexabromocyclododecane was provided by Japan (UNEP/FAO/RC/CRC.13/8 section 2.5.3.2 of the Japanese notification).

Norway:

A reference was provided to the document by the US EPA: Flame Retardant Alternatives for Hexabromocyclododecane. Final report June 2014. (UNEP/FAO/RC/CRC.13/8 section 2.5.3.2 of the Norwegian notification). The report provides information on hexabromocyclododecane used as a flame retardant in polystyrene building insulation, possible substitutes, and alternative materials. The report was developed by the U.S. Environmental Protection Agency with input from a partnership of stakeholders from business, government, academia, and environmental organizations. According to technical experts on the Partnership, between 2011 and 2014 there were only three viable flame retardant alternatives to HBCD for use in expanded and extruded polystyrene foam (EPS and XPS) insulation under current manufacturing processes. Alternative materials are also available as substitutes to HBCD-containing insulation. These alternatives may require additive flame retardants or other treatment to meet fire safety requirements. The Results section of that supporting document is reproduced below:

Results

Members of the Partnership identified many chemicals as potential alternatives; however, only three chemicals were identified as viable alternatives to hexabromocyclododecane in EPS and XPS foam: a butadiene styrene brominated copolymer (CASRN 1195978-93-8), a tetrabromobisphenol-A (TBBPA)-bis brominated ether derivative (CASRN 97416-84-7), and TBBPA-bis(2,3-dibromopropyl) ether (CASRN 21850-44-2). Only three alternatives were identified for evaluation in this report because flame retardants for EPS and XPS foam must allow the material to comply with fire safety codes while not compromising the performance of the foam. All three alternatives are brominated. No non-brominated flame retardants are known to be compatible in polystyrene manufacturing and associated flame tests. Figure ES-1 summarizes the hazard information for hexabromocyclododecane and the three alternatives assessed. (Figure ES-1 indicates whether endpoints were assigned based on empirical data or using values from predictive models and/or professional judgment. The caveats listed in Figure ES-1 must also be taken into account when interpreting the information in the table.) Few measured experimental data were available for the TBBPA-bis brominated ether derivative; therefore, estimated hazard designations were determined using TBBPA-bis(2,3-dibromopropyl ether) (CASRN 21850-44-2) as an analog.

ES 1 Hazard Summary for HBCD and Alternatives

VL = **Very Low hazard** L = **Low hazard** = **Moderate hazard** H = **High hazard** VH = **Very High hazard** — **Endpoints in colored text (***VL, L, M, H* **and** *VH***) were assigned based on empirical data. Endpoints in black italics (***VL, L, M, H,* **and** *VH***) were assigned using values from predictive models and/or professional judgment.**
This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

‡ This hazard designation would be assigned MODERATE for a potential for lung overloading if >% of the particles are in the respirable range as a result of dust forming operations.
§ Based on analogy to experimental data for a structurally similar compound.
♦ Aquatic toxicity: EPA DfE criteria are based in large part upon water column exposures which may not be adequate for poorly soluble substances such as many flame retardants that may partition to sediment and particulates.

Chemical For full chemical name and relevant trade names see the hazard profiles in Section 4.8	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Hexabromocyclododecane (HBCD)	25637-99-4 3194-55-6	L	M	L		H	M		L		VL	VL	VH	VH	H	VH
Butadiene styrene brominated copolymer[a]	119345-04-9	L	L	L	L	L	L	L[d]	L			L	L	L	VH	L
TBBPA bis brominated ether derivative[b]	97416-84-7	L	M	M	M	M	L	M	L		L	L	L	L	H	H
TBBPA bis(2,3-dibromopropyl) ether[b]	21850-44-2	L	M		M	M	L	M	L		L	L	L	L	VH	H

At this time, there are no standard test methods for respiratory sensitization and no test data; as a result there was no designation for this endpoint.

The human health endpoints evaluated in Design for Environment (DfE) alternatives assessments include acute toxicity, carcinogenicity, genotoxicity, reproductive toxicity, developmental toxicity, neurotoxicity, repeated dose toxicity, skin sensitization, respiratory sensitization, eye irritation, and dermal irritation. Hexabromocyclododecane has been assigned a "High" hazard designation for developmental neurotoxicity, a "Moderate" hazard designation for reproductive toxicity and repeated dose toxicity, and an estimated "Moderate" hazard designation for carcinogenicity and neurotoxicity; other health endpoints have "Low" or "Very Low" hazard designations. The butadiene styrene brominated copolymer has "Low" hazard designations (either measured or estimated) for most human health endpoints due to its high MW and limited potential for absorption; there is one "Moderate" hazard designation for the eye irritation endpoint based on experimental data. The TBBPA-bis brominated ether derivative and TBBPA-bis(2,3-dibromopropyl) ether have a "Moderate" hazard designation for carcinogenicity, mutagenicity, reproductive toxicity, developmental toxicity, and repeated dose toxicity based on potential alkylating properties. "Low" hazard designations have been assigned to these similar substances for acute toxicity, neurotoxicity, skin sensitization and irritation.

The ecotoxicity endpoints evaluated in DfE alternatives assessments include acute and chronic aquatic toxicities. Hexabromocyclododecane is toxic for the aquatic environment and has "Very High" hazard designations for both acute and chronic aquatic toxicity. Aquatic toxicity for the three alternatives is "Low", driven by their lack of appreciable water solubility leading to "no effects at saturation". Ecotoxicity data for terrestrial species was limited, and thus the potential for impacts on high trophic level and terrestrial wildlife from hexabromocyclododecane and its alternatives or associated degradation products is unclear.

The environmental fate of hexabromocyclododecane and the three alternatives is described primarily in terms of persistence and bioaccumulation potential. All three chemicals have "High" or "Very High" persistence designations, a quality typical for the majority of flame retardants. Long-term fate of the three alternatives in the environment is not well understood. The butadiene styrene brominated copolymer is estimated to have "Low" bioaccumulation potential due to its size (average MW >1,000 daltons) and lack of low MW components, while hexabromocyclododecane, the TBBPA-bis brominated derivative, and TBBPA-bis(2,3-dibromopropyl) ether have "Very High", "High", and "High" potential for bioaccumulation.

Under conditions where fire or incineration occurs, a halogenated substance may contribute to halogenated dibenzodioxin and dibenzofuran formation, increase the generation of polyaromatic hydrocarbons, and impact fire parameters such as smoke and carbon monoxide (Sidhu, Morgan et al. 2013). However, combustion reactions are complex and variable and make inclusion of combustion by-products in hazard assessment challenging. Both halogenated and non-halogenated flame retardants may yield other toxic by-products that would need to be compared, not only halogenated dioxins and furans. For these reasons, the pyrolysis transformation products are not assessed in this report.

In addition to the chemical hazard assessment of hexabromocyclododecane and its alternatives, Chapter 5 of the report includes general information about alternative insulation materials. These technologies include rigid board alternatives (e.g., similar to EPS and XPS), alternatives for certain functional uses (e.g., blanket insulation, foamed-in-place insulation), and specialty and emerging alternative materials (e.g., aerogel, carbon foam). The report does not assess these materials, does not compare them to EPS or XPS, and does not assess flame retardancy needs for each of these materials.

(UNEP/FAO/RC/CRC.13/INF/10)

General:

The POPs Review Committee of the Stockholm Convention has undertaken an evaluation of alternatives to hexabromocyclododecane during the Annex F (Risk Management Evaluation) phase of its review of hexabromocyclododecane as a candidate POP. The information can be found in the document titled *"Additional information on alternatives to hexabromocyclododecane and use in expanded polystyrene (EPS) and extruded polystyrene (XPS)"* (UNEP/POPS/POPRC.8/16/Add.3) available online at: http://chm.pops.int/Portals/0/download.aspx?d=UNEP-POPS-POPRC.8-16-Add.3.English.pdf

3.4 Socio-economic effects

Japan:

No information on socio-economic effects of the regulatory action was provided by Japan (UNEP/FAO/RC/CRC.13/8 section 2.5.3.1 of the Japanese notification).

Norway:

Hexabromocyclododecane has traditionally not been used in expanded polystyrene or extruded polystyrene for constructions buildings in Norway. Since these are the main uses of hexabromocyclododecane, low socio-economic effects are expected from of the final regulatory action.

(UNEP/FAO/RC/CRC.13/8 section 2.5.3.1 of the Norwegian notification)

4. Hazards and Risks to human health and the environment

4.1 Hazard Classification

WHO / IPCS	Not available.
IARC	Not available.
European Union	EU classification pursuant to Regulation (EC) No 1272/2008 on classification, labelling and packaging of substances and mixtures: Repr. 2, H361 (Suspected of damaging fertility or the unborn child) Lact., H362 (May cause harm to breast-fed children) (UNEP/FAO/RC/CRC.13/8 section 3.1 of the Norwegian notification)
US EPA	Not available.

4.2 Exposure limits

Studies establishing a tolerable daily intake for humans are not available.

There are several studies on reproductive effects of hexabromocyclododecane. Saegusa et al. (2009) performed a one-generation developmental toxicity study in rats, with maternal dietary exposure to 0, 100, 1,000 or 10,000 ppm hexabromocyclododecane from gestation day 10 until weaning of the offspring. The LOAEL of this study is 1,000 ppm (81-213 mg/kg/day), and the NOAEL 100 ppm (8-21 mg/kg/day). The long continuous exposure study of van der Ven et al. (2009) suggest that male reproductive organs are particularly sensitive to hexabromocyclododecane exposure, i.e. a decreased testicular weight was observed at a BMDL of 52 µg/g bw in F1 males. A weight reduction in other male organs; prostate, the adrenals, heart and brain as well as in F1 males' total weight was also observed. The observed body weight loss makes it impossible to say whether any of these effects on organs' weights are specific or secondary to the general body weight loss. In females the cytochrome P450 19 enzyme activity, based on group averages, showed a correlation to the internal concentration of γ- hexabromocyclododecane (linear correlation coefficient of 0.90). The cytochrome P450 19 enzyme converts androgens to estrogens (Norris 2006), and is essential for differentiation and development of gonads and brains of higher vertebrates, maintenance of reproductive tissues, and sexual behavior (Conley and Hinshelwood, 2001, Simpson et al. 2002). In females the time to vaginal opening was

also delayed, but only at the top dose (BMDL 82.2 µg/ g bw at a benchmark response (BMR) of 10%).
(UNEP/FAO/RC/CRC.13/INF/17/Rev.2 section 2.4.4 of the POPRC Risk Profile)

4.3 Packaging and labelling

The United Nations Committee of Experts on the Transportation of Dangerous Goods classifies the chemical in:

Hazard Class and Packing Group:	UN number: 3077 Proper shipping name and description: Hexabromocyclododecane, ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. Chemical name: Hexabromocyclododecane Class: 9 Classification code: M7 Packaging group: III Labels: 9 Remarks: Hazard identification No: 90 (ECHA Guidance on Safe Use – Hexabromocyclododecane)
International Maritime Dangerous Goods (IMDG) Code	UN number: 3077 Proper shipping name and description: Hexabromocyclododecane, ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. Chemical name: Hexabromocyclododecane Class: 9 Packaging group: III EmS number 1: F-A EmS number 2: S-F Labels: 9 Marine pollutant: yes (PP) (ECHA Guidance on Safe Use – Hexabromocyclododecane)
Transport Emergency Card	Not available.

4.4 First aid

NOTE: The following advice is based on information available from the World Health Organisation and the notifying countries and was correct at the time of publication. This advice is provided for information only and is not intended to supersede any national first aid protocols.

General: If you feel unwell seek medical advice (show this information or the container label where possible). Do not give anything by mouth to unconscious person.

Inhalation: Remove to fresh air. Seek medical attention immediately.

Skin: Remove any contaminated clothing, completely launder clothing to ensure that no contamination remains before reusing clothing. Wash skin thoroughly with soap and water for at least 15 minutes. If skin irritation occurs seek medical attention immediately.

Eye: Hold eyelids apart and flush eyes with plenty of water for at least 15 minutes. Seek medical attention.

Ingestion: If the subject is conscious rinse the mouth with water and make the subject drink 1 to 2 glasses of water, seek medical attention immediately.

(ECHA Guidance on Safe Use – Hexabromocyclododecane)

	Prevention	First Aid
Inhalation	Use ventilation. Use local exhaust.	Fresh air, rest.
Skin	Protective gloves. Protective clothing.	Rinse skin with plenty of water or shower.
Eyes	Wear safety spectacles.	First rinse with plenty of water for several minutes (remove contact lenses if easily possible), then refer for medical attention.
Ingestion	Do not eat, drink, or smoke during work. Wash hands before eating.	Rinse mouth.

IPCS (2001): International Chemical Safety Card (ICSC) 1413

4.5 Waste management

Technical guidelines on the environmentally sound management of wastes consisting of, containing or contaminated with hexabromocyclododecane:

- Best practice for the End-of-Life management of Polystyrene Foams in Building & Construction (European Chemical Industry Council (CEFIC) and PlasticsEurope, 2014;
- End-of-life treatment of HBCD-containing polystyrene insulation foams: Large-scale demonstration of the treatment of Expanded Polystyrene Foam (EPS) and Extruded Polystyrene Foam (XPS) containing Hexabromocyclododecane (HBCD) as a flame- retardant by co-incineration in the Würzburg Municipal Solid Waste Incinerator. Technical Summary report (PlasticsEurope, 2015)
- HBCD Hexabromocyclododecane in Polystyrene Foams Product Safety Assessment - 2016 Edition

Source: Basel Convention POPs Waste, Additional Resources

DISPOSAL: Dispose of as hazardous waste in compliance with local, regional and national regulations. Dispose of wastes in an approved waste disposal facility.

Source: Source: ECHA Guidance on Safe Use – Hexabromocyclododecane

Annexes

Annex 1	**Further information on the substance**
Annex 2	**Details on final regulatory action reported**
Annex 3	**Address of designated national authorities**
Annex 4	**References**

Annex 1 Further information on the substance

Introductory text to Annex 1

The information presented in the present annex reflects the conclusions of the two notifying Parties, namely Japan and Norway. Where possible, information provided by these two Parties on hazards has been presented together, while the risk assessments, which are specific to the conditions prevailing in the Parties, are presented separately. This information is taken from the documents referenced in the notifications in support of the final regulatory actions relating to hexabromocyclododecane.

The notifications from Japan and Norway were first reported in PIC Circular XLIV of 12/12/2016.

Annex 1 – Further information on *notified chemical*

1.	**Identity and Physico-Chemical properties**	
1.1	**Identity**	Hexabromocyclododecane and 1,2,5,6,9,10 –hexabromocyclododecane (UNEP/FAO/RC/CRC.13/INF/17/Rev.2, POPRC Risk Profile)
1.2	**Formula**	$C_{12}H_{18}Br_6$ (UNEP/FAO/RC/CRC.13/INF/17/Rev.2, POPRC Risk Profile)
1.3	**Colour and Texture**	White odourless solid (UNEP/FAO/RC/CRC.13/INF/17/Rev.2, POPRC Risk Profile)
1.4	**Decomposition temperature**	Decomposes at >190 °C (UNEP/FAO/RC/CRC.13/INF/17/Rev.2, POPRC Risk Profile)
1.6	**Density (g/cm³)**	2.38 Albemarle Corporation (1994) 2.24 Great Lakes Chemical Corporation (1994) (UNEP/FAO/RC/CRC.13/INF/17/Rev.2, POPRC Risk Profile)
1.7	**Resistance to acids**	Not available.
1.8	**Resistance to alkalis**	Not available.
1.9	**Tensile strength (10^3 kg/cm²)**	Not available.

2	**Toxicological properties**	
2.1	**General**	
2.1.1	**Mode of Action**	Recent studies with fish models suggest that hexabromocyclododecane may induce oxidative stress and apoptosis. (UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 2.4.1 of the POPRC Risk Profile).
2.1.2	**Symptoms of poisoning**	Not available.
2.1.3	**Absorption, distribution, excretion and metabolism in mammals**	Absorption: The extent of oral absorption of hexabromocyclododecane in humans is largely unknown (ECHA 2008a). Estimations suggest that the uptake of hexabromocyclododecane via this exposure route ranges from 50-100% (ECHA 2008a, European Union 2008). According to calculations made in the EU risk assessment (European Union 2008) intake of hexabromocyclododecane via breast milk is 1.5 ng/ kg bw/ day for 0-3 month olds and 5.6 ng/ kg bw/ day in 3-12 month old babies. However, with the levels found in mothers' milk from some locations in northern Spain (A Coruña), Eljarrat et al. 2008 calculated the intake to be 175 ng/ kg bw/day for 1 month olds. This is 12 times higher than the estimated daily intake (EDI) for 0-3 month old infants as determined in the EU risk assessment (European Union 2008) and 25-1,458 times higher than the EDI for adults in Sweden, Netherlands, United Kingdom and Norway (KEMI, 2009; Eljarrat et al. 2009, Roosens et al. 2010). A Flemish dietary study suggests that the age group between 3 and 6 years seems to be the highest exposed with an EDI for the sum of hexabromocyclododecane isomers of 7 ng/kg bw day. Newborns and adults are less exposed with EDI's of 3 and 1 ng/kg bw day, respectively (Roosens et al. 2010). In all instances, however, children appear to be more exposed than adults. (UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 2.3.2 of the POPRC Risk Profile) Distribution: Hexabromocyclododecane can be absorbed from the gastro-intestinal tract, and the highest concentrations are subsequently reached in adipose tissue and muscles followed by liver, and with much lower activities present in lung, kidney, blood, brain, and gonads. (UNEP/FAO/RC/CRC.13/8 section 3.2.2 of the Norwegian notification) In rodents, hexabromocyclododecane is readily absorbed through the

gastrointestinal tract with highest concentrations in adipose tissue and muscle, followed by the liver; it has been found in much lower concentrations in the lungs, kidneys, blood and brain. (ECHA, 2008; reported in a secondary source with limited study details.)

(UNEP/FAO/RC/CRC.13/INF/18 US EPA: Flame Retardant Alternatives for Hexabromocyclododecane (HBCD)).

Bioaccumulation and metabolism:

Several studies in laboratory, in local food webs and local ecosystems confirm the potential for hexabromocyclododecane to bioaccumulate and biomagnify. The field studies show a general increase of concentrations in biota with increasing trophic level in aquatic and Arctic food webs. No field studies in the terrestrial environment have been identified, but two laboratory studies show that hexabromocyclododecane has a potential to bioaccumulate in terrestrial mammals.

Two studies in the laboratory have examined the bioaccumulation of hexabromocyclododecane in mammals (WIL 2001; Velsicol Chemicals 1980). In a 90-day repeated dose (technical hexabromocyclododecane, 1,000 mg/kg bw/day) toxicity study with rats, WIL (2001) found that concentrations of the α-isomer were much greater than that of the β- and γ-isomers at all sampling time points. The relative percentage of the isomers measured in the rats (α-: 65-70%; β-: 9-15% and γ-: 14-20%) was markedly different to the proportions in the hexabromocyclododecane formulation used (α-: 8.9%; β-: 6.6% and γ-: 84.5%). Velsicol Chemicals (1980) studied the pharmacokinetics of radiolabelled hexabromocyclododecane (14C-hexabromocyclododecane, purity > 98%) administered to rats as a single oral dose. The authors found that the test substance was distributed throughout the body with the greatest amounts measured in fat tissue, followed by liver, kidney, lung and gonads. Rapid metabolism to polar compounds occurred in the blood, muscle, liver and kidneys, but hexabromocyclododecane remained mostly unchanged in the fatty tissue. The study concluded that hexabromocyclododecane accumulated in fatty tissues following repeated exposure.

Findings have been made in the Norwegian Arctic. Sørmo et al. (2006) analyzed representative species from different trophic levels of the polar bear food chain, using samples collected from 2002 to 2003 at Svalbard in the Norwegian Arctic. hexabromocyclododecane was below detection limits (minimum 0.012 ng/g lw) in the amphipod, *Gammarus wilkitzkii*. Hexabromocyclododecane biomagnified strongly from polar cod (*Boreogadus saida*) to ringed seal (BMF of 36.4, based on whole body wet weight concentrations), but did not biomagnify from ringed seal to polar bear (BMF of 0.6). Lower levels in the polar bear samples were considered to indicate possible enhanced metabolic capability in the bears. In East Greenland the comparative bioaccumulation, biotransformation and/or biomagnification from East Greenland ringed seal (*Pusa hispida*) blubber to polar bear (*Ursus maritimus*) tissues (adipose, liver and brain) of hexabromocyclododecane and legacy POPs was investigated by Letcher et al. (2009). α-hexabromocyclododecane was found to only bioaccumulate in the polar bear adipose tissue. The ringed seal blubber to polar bear adipose BMF for total-(α)- hexabromocyclododecane >1. The authors concluded that even if the metabolism of hexabromocyclododecane in polar bears was enhanced compared to other species, the high exposure of hexabromocyclododecane ensures biomagnification.

Morris et al. (2004) reported on biomagnification of hexabromocyclododecane in the North Sea food web. Although individual BMFs were not reported, the authors suggested that because concentrations of hexabromocyclododecane were higher in species in the top of the food chain it implied that hexabromocyclododecane was biomagnifying. For example, hexabromocyclododecane concentrations in top predators such as harbour seals (*Phoca vitulina*) and harbour porpoise (*Phocoena phocoena*) were several orders of magnitude greater than those measured in the aquatic macroinvertebrates such as sea-star and common whelk. Similarly,

hexabromocyclododecane concentrations were high in liver samples from cormorant, a predator bird-species and in eggs of the common tern, while lower levels of hexabromocyclododecane were detected in their prey, cod and yellow eel (*Anguilla Anguilla*).

Tomy et al. (2008) investigated isomer-specific accumulation of hexabromocyclododecane at several trophic levels of an eastern Canadian Arctic marine food web. There was a significant positive relationship of α-hexabromocyclododecane with trophic level, with a TMF of 7.4 ($p<0.01$), indicative of biomagnification throughout the food web, while a significant negative relationship was observed between concentrations of γ-hexabromocyclododecane and trophic level (i.e. trophic dilution). α-hexabromocyclododecane contributed greater than 70% of the total hexabromocyclododecane burden in shrimp (*Pandalus borealis, Hymenodora glacialis*), redfish (*Sebastes mentella*), arctic cod (*Boreogadus saida*), narwhal (*Monodon monoceros*) and beluga (*Delphinapterus leucas*), while γ-hexabromocyclododecane was greater than 60% of total hexabromocyclododecane in zooplankton (mix), clams (*Mya truncata, Serripes groenlandica*), and walrus (*Odobenus rosmarus*). The observed differences in diastereoisomer predominance were attributed in part to differing environmental fate and behaviour of the isomers, with the least water soluble γ-isomer more likely to diffuse passively from the water column into zooplankton, which have proportionately high lipid content. Similarly, as benthic filter feeders, clams may be more likely to absorb a higher proportion of the γ-isomer from sediment. The presence of higher proportions of α-hexabromocyclododecane, such as with the beluga and narwhal, may indicate enhanced metabolic capability based on evidence of stereoisomer-specific biotransformation of the γ-isomer to the α-form (Zegers et al. 2005, Law et al. 2006d). This also corresponds with the findings of Tomy et al. (2009) where the α-isomer accounted for >95% of the overall burden of hexabromocyclododecanes in the beluga, while the Arctic cod, the primary prey species of beluga in the western Canadian arctic marine food web, had a hexabromocyclododecane-profile dominated by the γ-isomer (>77%). The authors concluded that this was further evidence that beluga can bioprocess the γ- to the α-isomer.

In vivo studies with rats suggest that hexabromocyclododecane is also debrominated to PBCDe and TBCDe. In total, five different species of hydroxylated hexabromocyclododecane metabolites have been found by LCQ and GC-MS; monohydroxy- and dihydroxy-hexabromocyclododecane, monohydroxy- and dihydroxy-PBCDe and monohydroxy-TBCDe (Brandsma et al. 2009).

(UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 2.2.2 of the POPRC Risk Profile)

Excretion:

Hexabromocyclododecane is excreted mainly through faeces with minor elimination in urine, and three polar metabolites as well as unextractable radioactivity have been detected. Elimination from body fat appears to be markedly slower than from other tissues, with an elimination half-life of the three diastereomers possibly being in the order of weeks to months.

(UNEP/FAO/RC/CRC.13/8 section 3.2.2 of the Norwegian notification)

Rats (2 males, 8 females) administered a single oral dose of 1.93 mg radiolabeled hexabromocyclododecane eliminated 86% of the dose within 72 hours (70% in feces and 16% in urine). (EPA, 2005; NICNAS, 2012; reported in a secondary source. Authors state that caution is urged in interpreting the data due to the small sample size and the brief nature of the final report.)

Four male Wistar rats orally administered 500 mg/kg-day hexabromocyclododecane in olive oil for 5 days Average daily rate of excretion in the feces was 29-37% of the dose; the cumulative excretion was constant at 32-35%; urinary excretion was not observed; metabolites were not detected in the urine or feces;

hexabromocyclododecane was detected only in adipose tissue (0.3-0.7 mg/g fat). (EPA, 2005; NICNAS, 2012, reported in a secondary source.)

(UNEP/FAO/RC/CRC.13/INF/18 US EPA: Flame Retardant Alternatives for Hexabromocyclododecane (HBCD)).

2.2 Toxicology studies

2.2.1 Acute toxicity

Oral:

Rat LD_{50} > 10,000 mg/kg (EPA, 2005; NICNAS, 2012; reported in a secondary source with limited study details.)

Rat LD_{50} > 6,400 mg/kg (EINECS, 2008; reported in a secondary source. Non-guideline study. Dose and particle size not reported; 7-day observation period.)

Dermal:

Rabbit LD_{50} > 8,000 mg/kg (EPA, 2005; NICNAS, 2012; reported in a secondary source with limited study details)

Rabbit LD_{50} > 20,000 mg/kg (EINECS, 2008; NICNAS, 2012; non-guideline study. Too few animals were used; clinical signs not reported.)

Inhalation:

Rat LC_{50} > 200 mg/L (EPA, 2005; NICNAS, 2012; reported in a secondary source with limited study details.)

(UNEP/FAO/RC/CRC.13/INF/18 US EPA: Flame Retardant Alternatives for Hexabromocyclododecane (HBCD)).

2.2.2 Short term toxicity

Not available for mammals/vertebrates.

2.2.3 Genotoxicity (including mutagenicity)

Gene mutation *in vitro*:

Negative in *Salmonella typhimurium* (strains not specified) in the presence and absence of metabolic activation. (EPA, 2005; NICNAS, 2012; reported in a secondary source with limited study details.)

Chromosomal aberrations *in vitro*:

Negative, mammalian chromosomal aberration test with human peripheral blood lymphocytes in the presence and absence of metabolic activation

- Doses: 10, 19, 38, 75, 150, 300 and 600 µg/mL.

(EPA, 2005; NICNAS, 2012; . Guideline study. Performed according to current EPA, OECD guidelines, and GLP.)

Other *in vitro*:

Positive, intragenic recombination test in Sp5/V79 and SPD8 hamster cells; cell lines developed by study authors.

- Doses: 2-20 µg/mL.

(EPA, 2005; NICNAS, 2012; reported in a secondary source. Non-guideline study. Not a standard test used by regulatory agencies to assess genotoxicity. Reliability and predictive ability is unknown.)

Negative, mouse micronucleus test.

- Doses: 0, 500, 1,000 or 2,000 mg/kg in dimethyl sulfoxide.

(EPA, 2005; reported in a secondary source. Guideline study. Performed according to current EPA, OECD guidelines and GLP.)

(UNEP/FAO/RC/CRC.13/INF/18 US EPA: Flame Retardant Alternatives for Hexabromocyclododecane (HBCD)).

2.2.4 Long term toxicity and carcinogenicity

The EU risk assessment of hexabromocyclododecane completed in 2008 provides the most comprehensive assessment of toxic effects and risks of hexabromocyclododecane exposure to human health and welfare (European Union 2008). This assessment concludes that hexabromocyclododecane may cause

reproductive toxicity and long term toxicity, whereas there is no concern for acute toxicity, irritation, sensitization, mutagenicity and carcinogenicity.

(UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 2.4.5 of the POPRC Risk Profile).

Repeated dose studies with oral exposure in rats and mice resulted in increased liver weight and effects on the pituitary weight and thyroid hormone parameters. A LOAEL of 22.5 mg/kg was proposed for repeated dose.

(UNEP/FAO/RC/CRC.13/8 section 3.2.2 of the Norwegian notification).

2.2.5 Effects on reproduction

There are several studies on reproductive effects of hexabromocyclododecane. Saegusa et al. (2009) performed a one-generation developmental toxicity study in rats, with maternal dietary exposure to 0, 100, 1,000 or 10,000 ppm hexabromocyclododecane from gestation day 10 until weaning of the offspring. In this study thyroid effects were observed both in dams (thyroid weight increase and follicular cell hypertrophy at 10,000 ppm) and offspring (thyroid weight increase, decreased serum T3 and increased serum TSH at 1,000 and 10,000 ppm). The thyroid effects together with the impaired oligodendroglial development in the brain cortex (statistically significant at the high dose (-24%) supported by a dose-dependent trend in the mid (-12%) and low (-8%) dose groups) and the decreased female body weight (9% in the high dose group) could indicate developmental hypothyroidism. The LOAEL of this study is 1,000 ppm (81-213 mg/kg/day), and the NOAEL 100 ppm (8-21 mg/kg/day). The long continuous exposure study of van der Ven et al. (2009) suggest that male reproductive organs are particularly sensitive to hexabromocyclododecane exposure i.e. a decreased testicular weight was observed at a BMDL of 52 µg/ g bw in F1 males. A weight reduction in other male organs: prostate, the adrenals, heart and brain as well as in F1 males' total weight was also observed. The observed body weight loss makes it impossible to say whether any of these effects on organs' weights are specific or secondary to the general body weight loss. In females the cytochrome P450 19 enzyme activity, based on group averages, showed a correlation to the internal concentration of γ-hexabromocyclododecane (linear correlation coefficient of 0.90). The cytochrome P450 19 enzyme converts androgens to estrogens (Norris 2006), and is essential for differentiation and development of gonads and brains of higher vertebrates, maintenance of reproductive tissues, and sexual behavior (Conley and Hinshelwood, 2001, Simpson et al. 2002). In females the time to vaginal opening was also delayed, but only at the top dose (BMDL 82.2 µg/ g bw at a benchmark response (BMR) of 10%).

Like the studies of van der Ven et al. (2009) and Saegusa et al. 2009, Ema et al. (2008) document reproductive and developmental effects (decreased pup viability, fewer primordial follicles), and also changes in organ weights (e.g. liver and thyroid), and thyroid hormone levels. Several effects were trans-generational and affected both F0 parents and F1 and F2 parents and offspring. From the point of view of reproductive toxicology, the general decrease in viability in F2 pups on post-natal days 4 and 21 at 1,500 and 15,000 ppm and the decrease in primordial follicles at 1,500 and 15,000 ppm hexabromocyclododecane exposure in F1 females were the most severe effects. A reduced number of primordial follicles suggests that reproductive potential of the female may be reduced, and is generally regarded as sensitive biomarkers for adverse reproductive effects (Parker et al. 2006). It should be noted however that the highest dose used by Ema et al. (2008) may be considered to be very high. However, dosing was in this study done by mixing hexabromocyclododecane particles into an appropriate amount of powdered basal diet for each dietary concentration. The absorption kinetics of hexabromocyclododecane likely depends on both the particle size and amount of particles administered, and is expected to be lower than for dissolved hexabromocyclododecane. The actual tissue doses from this study are therefore presumably lower than the original dose would suggest, as may also be assumed from the findings of similar studies such as that of WIL 2001 who only observed reversible effects at doses up to 1,000 mg/kg bw/day in their 90-day oral exposure study.

(UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 2.4.4 of the POPRC Risk Profile)

A NOAEL of 10 mg/kg/day has been deduced in a two-generation reproductive toxicity study in rats. The NOAEL is based on dose-dependent decrease in fertility index and a reduced number of primordial follicles. Other effects observed were effect on liver and thyroid weight and TSH hormone level, and increased mortality during lactation.

Neonatal hexabromocyclododecane exposure may cause developmental neurotoxic effects as illustrated by statistically significant changes in spontaneous behaviour, learning and memory defects. Male mice exposed orally with a single dose at day 10 postnatal (brain growth spurt in mice), were tested for behaviour effects at 3 months age. Clear effects were seen on all parameters tested at 13.5 mg/kg, and on some at 0.9 mg/kg, giving an indicative LOAEL of 0.9 mg/kg/day from this study (Eriksson et al., 2006, as described in the EU Risk assessment for HBCD 2008). Hexabromocyclododecane inhibited the high affinity uptake of neurotransmitters (dopamine and glutamate) into synaptosomes at similar concentration levels as previously shown for polychlorinated biphenyls (PCBs) (Mariussen and Fonnum, 2003, as described in the EU Risk assessment for HBCD 2008).

(UNEP/FAO/RC/CRC.13/8 section 3.2.2 of the Norwegian notification).

2.2.6 Neurotoxicity/ delayed neurotoxicity, Special studies where available

Thyroid hormones are required for normal development of the nervous system, as are retinoids (Forrest et al. 2002, Maden 2007), and disturbances in these systems may therefore result in long term neurotoxic effects in off-spring. For hexabromocyclododecane, a neurotoxic potential has previously been indicated both *in vivo* and *in vitro* with rodent models (Reistad et al. 2006, Mariussen and Fonnum, 2003, Dingemans et al. 2009, Eriksson et al. 2006, Lilienthal et al. 2009). In the *in vivo* study of Eriksson et al. (2006) neonatal direct exposure of pups to a single oral dose of hexabromocyclododecane (0.9 mg/ kg or 13.5 mg/ kg bw on postnatal day 10), induced alterations in spontaneous behavior with initial hypo-reactivity, followed by impaired habituation in adult mice. This study also reported effects on spatial learning and memory as assessed in a Morris water maze test with exposed mice. In contrast, in their two-generation study with rats where exposure of pups occurred indirectly via human breast milk, Ema et al. (2008), only observed transient changes in the performance of F1 males in a water-filled T-maze test at an exposure level of 1,500 ppm and higher and no effects on other parameters (locomotor activity). According to Ema et al. (2008), the discrepancy in their results from the results obtained in previous studies could be explained by differences in exposure regime and/or by differences in species sensitivity. Results from *in vitro* studies suggest that hexabromocyclododecane may be cytotoxic to nerve cells and possibly also interfere with neuronal signalling events such as Ca^{2+} and neurotransmitter uptake (Reistad et al. 2006, Mariussen and Fonnum 2003, Dingemans et al. 2009).

The *in vivo* neurotoxic potential of hexabromocyclododecane has also been studied by Lilienthal et al. 2009. In a one generation reproduction feeding study, they showed that hexabromocyclododecane-induced loss in hearing function was paralleled by changes in dopamine dependent behaviour (Lilienthal et al. 2009). Loss of hearing function was attributed to a cochlear effect of hexabromocyclododecane that resulted in increased thresholds and moderate prolongations of latencies in the lower frequency range from 0.5 to 2 kHz and after clicks. Both observed effects were dose-dependent with lower bounds of bench mark doses (BMDL) between ≤ 1 and 10 mg/ kg bw. Saegusa et al. (2009) on the other hand detected weak hypothyroidism with increases in thyroid weight, thyroid follicular cell hypertrophy and serum TSH concentrations as well as a decrease in serum T3 levels in rat off-spring exposed to 10,000 ppm hexabromocyclododecane in a soy-free diet from gestation day 10 to day 20 after delivery. The TH changes were accompanied by a reduced density of CNPase-positive oligodentrocytes, which is indicative of impaired oligodendroglial development. Increased thyroid weights and decreased serum T3 concentrations were also observed in the adult stage from 1,000 ppm. Though the above data suggest that hexabromocyclododecane induced disturbances in TH-signalling is linked to effects on the nervous system in rodents, changes in behaviour and cognition may also be

impacted by a decrease in apolar retinoids as observed in female rat livers following hexabromocyclododecane exposure (van der Ven et al. 2006, van der Ven et al. 2009). Moreover, the interferences of hexabromocyclododecane with sex-steroid hormones and their receptors should not be neglected as these hormones also exert non-genomic effects on brain functions such as learning and memory, fine motor control, pain perception and mood (Boulware and Mermelstein 2005, Chakraborti et al. 2007, Meaney et al. 1983, Schantz and Widholm 2001).

(UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 2.4.4 of the POPRC Risk Profile).

2.2.7 Summary of mammalian toxicity and overall evaluation

Hexabromocyclododecane exerts reproductive, developmental and neurotoxic effects in mammals with a NOEC/NOAEL in the order of 1 mg/kg/day. *In vivo* data include:

- Decreased pup survival and fewer primordial follicles in rats at 100 mg/kg/day, NOAEL 10 mg/kg/day (Ema et al. 2008).
- Decreased pup weight, decreased testis and prostrate weights, impaired hearing, and reduction in female bone mineral density in rat offspring at 30-100 mg/kg/day (van der Ven et al. 2009, Lillienthal et al. 2009).
- TH imbalance and impaired oligodendroglial development in the brain cortex of rat offspring at 1,000 ppm (81-213 mg/kg/day), NOAEL 8-21 mg/kg/day (Saegusa et al. 2009).
- Behavioural effects in mice exposed to 13.5 mg/kg/day at day 10, NOAEL 0.9 mg/kg/day (Eriksson et al. 2006).

(UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 3 of the POPRC Risk Profile)

3 Human exposure/Risk evaluation

3.1 Food

In humans hexabromocyclododecane is found in blood, plasma and adipose tissue. The main sources of exposure presently known are contaminated food and dust. For breast feeding children, mothers' milk is the main exposure route but hexabromocyclododecane exposure also occurs at early developmental stages as it is transferred across the placenta to the foetus. Human breast milk data from the 1970s to 2000 show that hexabromocyclododecane levels have increased since hexabromocyclododecane was commercially introduced as a brominated flame retardant in the 1980s. Though information on the human toxicity of hexabromocyclododecane is to a great extent lacking, and tissue concentrations found in humans are seemingly low, embryos and infants are vulnerable groups that could be at risk, particularly to the observed neuroendocrine and developmental toxicity of hexabromocyclododecane.

(UNEP/FAO/RC/CRC.13/INF/17/REV.2 Executive Summary of the POPRC Risk Profile)

Reported dietary exposure levels in humans vary globally and regionally (Shi et al. 2009, Roosens et al. 2009). Surveys in Europe and the US reveal dietary exposure levels for hexabromocyclododecane in the range of <0.01-5 ng/g w/w (see Roosens et al. 2009 for overview). Fatty foods of animal origin such as meat and fish are likely a major source of dietary human exposure, and the exposure situation closely depends on the consumption of those products in the population (e.g. Shi et al. 2009; Remberger et al. 2004, Lind et al 2002, Driffield et al. 2008). Among all dietary samples, the highest hexabromocyclododecane concentrations (up to 9.4 ng/g w/w) are reported for fish (Knutsen et al. 2008, Remberger et al. 2004, Allchin and Morris 2003). Accordingly in Norway, where fish is an important part of the diet, intake of fish has been found to closely correlate with serum hexabromocyclododecane levels (Thomsen et al. 2008; Knutsen et al. 2008). Eggs are another potential source of human exposure (Hiebl et al. 2007, Covaci et al. 2009). A survey of home-grown chicken eggs sampled near contaminated sites in developing countries showed eggs to contain <3.0-160 ng/g lipid weight (IPEN, 2005), hexabromocyclododecane levels in eggs were high in Mexico (91 ng/g lipid), Uruguay (89 ng/g lipid), Slovakia (89 ng/g lipid), relatively high in Turkey (43 ng/g lipid), and extremely high in Kenya (160 ng/g lipid). That vegetables may contain hexabromocyclododecane at similar concentrations as have been reported for meat and fish, was shown by Driffield et al. (2008), who assessed 19 different food

		groups representing the UK diet for 2004 for brominated flame retardants. The presence of hexabromocyclododecane in vegetables and vegetable oils and fats may arise from the presence of this substance in sewage sludge and the subsequent use of sewage sludge as a food crop fertilizer (Kupper et al. 2008, Brändli et al. 2007). Stereoisomeric patterns in food samples suggest both global and regional variation, as well as stereoisomeric differences depending on food type (Roosens et al. 2009; Shi et al. 2009). (UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 2.3.2 of the POPRC Risk Profile)
3.2	**Air**	A study by Abdallah et al (2009) found hexabromocyclododecane in household air (median concentration 180 pg m-3), household dust (median concentration 1,300 ng/g), offices (median concentration 760 ng/g), and cars (median concentration 13,000 ng/g). (UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 2.3.2 of the POPRC Risk Profile)
3.3	**Water**	Not available.
3.4	**Occupational exposure**	In the work environment direct dermal exposure and inhalation of fine hexabromocyclododecane dust or particles are particular concerns. In a study by Thomsen et al. (2007) industrial workers at plants producing EPS with hexabromocyclododecane were found to have elevated hexabromocyclododecane levels in their blood (i.e. 6-856 ng/g lw serum). Serum/blood levels in non-occupationally exposed individuals are typically much lower (i.e. 0.005-6.9 ng/g lw) though the data indicates potentially significant sources of exposure (see KEMI 2008 for overview). (UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 2.3.2 of the POPRC Risk Profile)
3.5	**Medical data contributing to regulatory decision**	Not available.
3.6	**Public exposure**	In non-occupationally exposed individuals indirect exposure via the environment or products, be it oral, dermal or by inhalation, is the main concern. In a study by Stapleton et al. (2008) hexabromocyclododecane levels in dust samples from indoor environments ranged from <4.5 ng/g to a maximum of 130,200 ng/g with a median value of 230 ng/g. As a result of continuous exposure in homes, offices and cars, hexabromocyclododecane is found in human adipose tissue (Pulkrabová et al. 2009; Johnson-Restrepo et al. 2008; Antignac et al. 2008; Abdallah and Harrad 2009) and blood (Weiss et al. 2004; Weiss et al. 2006; Lopez et al. 2004; Brandsma et al. 2009; Thomsen et al. 2007; Meijer et al. 2008; Roosens et al. 2009). Exposure occurs at an early stage of development as hexabromocyclododecane is transferred across the human placenta to the fetus (Mejier et al. 2008), and is also transferred from mother to child via breast milk. Hexabromocyclododecane has been detected in breast milk in Europe (Covaci et al. 2006; Lignell et al. 2009; Eljarrat et al. 2009; Colles et al. 2008; Polder et al. 2008a; Polder et al. 2008b; Fängström et al. 2008; Antignac et al. 2008), in Asia (Kakimoto et al. 2008; Shi et al. 2009; Malarvannan et al. 2009; Tue et al. 2010), in Russia (Polder et al. 2008b), Mexico (Lopez et al. 2004) and in USA (Schecter et al. 2008). Hence exposure to hexabromocyclododecane occurs at critical stages of human development, both during pregnancy and postnatally via breast milk. Reported concentrations of hexabromocyclododecane in breast milk range from below detection limit to 188 ng hexabromocyclododecane/g lw (for overview see European Union 2008). According to EBFRIP 2009b the typical range of total hexabromocyclododecane concentrations in human breast milk in populations inhabiting industrialized areas appears to be <1 to 5 ng/g lw. Geographically, the highest hexabromocyclododecane levels have been found in mothers' milk from two areas in Northern Spain (Catalonia and Galicia). The reported hexabromocyclododecane levels from these studies ranged from 3-188 and 8 -188 ng/g lw, with median values of 27 and 26 ng/g lw, respectively (Eljarrat et al. 2009; Guerra et al. 2008a). (UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 2.3.2 of the POPRC Risk Profile)

3.7 Summary-overall risk evaluation

The EU risk assessment of hexabromocyclododecane completed in 2008 provides the most comprehensive assessment of toxic effects and risks of hexabromocyclododecane exposure to human health and welfare (European Union 2008). This assessment concludes that hexabromocyclododecane may cause reproductive toxicity and long term toxicity, whereas there is no concern for acute toxicity, irritation, sensitization, mutagenicity and carcinogenicity. It moreover states that hexabromocyclododecane poses no risk to adult consumers or to workers when standard industrial hygiene measures are applied (current EU practice). These conclusions are founded on an extensive list of toxicity studies and on a comprehensive selection of exposure and risk assessments that consider not only workers and adult consumers, but also indirect exposure of humans via the environment (European Union 2008). The EU risk assessment documents that currently in the general (human) population, hexabromocyclododecane tissue concentrations are much below those reported to induce adverse effects in other mammals (European Union 2008).

The substance is suspected of damaging fertility or the unborn child (Repr. 2: H361), and the substance may cause harm to breast-fed children (Lact.: H362) (KEMI 2009).

Significant levels of hexabromocyclododecane in human milk and exposure through food has been reported near local sources. In humans the main risks of hexabromocyclododecane exposure are possible neuroendocrine and developmental disturbances from exposure during the early developmental phases of the child.

(UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 2.4.5 of the POPRC Risk Profile).

In humans, the main risks of hexabromocyclododecane exposure are possible neuroendocrine and developmental disturbances from exposure during the early developmental phases of the child.

In addition to the findings in the *in vivo* animal studies, there are a large number of recent *in vitro* studies that document how hexabromocyclododecane upon adsorption may act on, and possibly interfere with biological processes such as cell homeostasis, protein repair, metabolism, intracellular signalling and neuroendocrine processes. Such studies add to the understanding that exposure to hexabromocyclododecane has various effects on human health and the environment, and should also be regarded when considering the toxicity of hexabromocyclododecane.

(UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 3 of the POPRC Risk Profile).

4 Environmental fate and effects

4.1 Fate

4.1.1 Soil

The rate of degradation of hexabromocyclododecane is slower in the presence of oxygen. Davis et al. (2005) reported on the biodegradation of technical hexabromocyclododecane in freshwater sediments and soils. Using OECD test guidelines 307 and 308, the authors demonstrated that the rate of loss of hexabromocyclododecane at 20°C was appreciably faster under anoxic conditions in both media. Relative to biologically sterile controls, biotransformation of hexabromocyclododecane was faster in the presence of microorganisms and DT_{50} values ranged from 11 to 32 days (aerobic) and 1.1 to 1.5 days (anaerobic) in sediment. In soil, half-lives under aerobic and anaerobic conditions were 63 and 6.9 days, respectively. However, in this study only the degradation of γ-hexabromocyclododecane was studied since the test concentration was too low to allow detection of α- and β-hexabromocyclododecane. It was also not possible to detect transformation products.

In the EU Risk Assessment, the degradation half-lives in aerobic sediment were calculated at 20°C to be 113, 68 and 104 days for α-, β- and

γ-hexabromocyclododecane, respectively (European Union 2008). In sediment, technical-hexabromocyclododecane was observed to be subject to primary degradation with half-lives of 66 and 101 days in anaerobic and aerobic sediment at 20°C, respectively. The EU Risk Assessment notes that the study was conducted at hexabromocyclododecane concentrations much greater (mg/kg) than Davis et al. (2005) (µg/kg), so the degradation kinetics may be limited by the mass transfer of chemical into the microbes. The main transformation product was 1,5,9-cyclododecatriene (CDT) which was formed via a step-wise reductive dehalogenation of hexabromocyclododecane. No CO_2 was detected during the study. However, in a study performed according to OECD guideline 301F (Davis et al. 2006b), it was shown that t,t,t-CDT can be degraded to CO_2.

Degradation rate constants of hexabromocyclododecane, under anaerobic conditions in sewage sludge have also been reported (Gerecke et al. 2006). Experiments were conducted by adding individual target compounds or mixtures to freshly collected digested sewage sludge. The sewage sludge was amended with yeast and starch. Experiments, performed at 37°C, with racemic mixtures of individual diastereoisomers showed that (+/-)-β-hexabromocyclododecane and (+/-)-γ-hexabromocyclododecane degraded faster than (+/-)-α-hexabromocyclododecane by an estimated factor of 1.6 and 1.8, respectively. Based on the investigations of Davis et al. (2006a) and Gerecke et al. (2006), α-hexabromocyclododecane seems to be subject to a slower degradation than β- and γ-hexabromocyclododecane.

(UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 2.2.1 of the POPRC Risk Profile).

4.1.2 Water

There are no reliable empirical data on the degradation kinetics of hexabromocyclododecane in water. The hydrolysis of hexabromocyclododecane has not been studied. Hydrolysis should however, not be considered as a significant route of environmental degradation for this substance due to the low water solubility, the high partitioning to organic carbon, and the lack of hydrolysable functional groups (OECD 2007). According to calculations in the EMEP report on hexabromocyclododecane, the physical-chemical properties of the technical mixture and γ-hexabromocyclododecane stereoisomer give a half-life in water of about 5 years (EMEP 2009).

According to EBFRIP (2009b) the half-life for water and soil derived from comparing different model estimations lies in the range 8.5 – 850 days, with a median of 85 days and confidence factor (CF) of 10. The half-life in freshwater and marine sediments lies in the range 6 – 210 days, with a median of 35 days and CF of 6. EBFRIP (2009b) does not differentiate between fresh water and marine sediment.

(UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 2.2.1 of the POPRC Risk Profile).

4.1.3 Air

The atmospheric degradation half-life of hexabromocyclododecane by gas-phase reaction with hydroxyl radicals (OH) has not been experimentally measured but can be modeled, providing an estimate (by AopWin v1.91) of 76.8 hours (3.2 days). The estimate was obtained by assuming a concentration of 5×10^5 OH molecules·cm^{-3} and that the reaction takes place 24 hours a day (these are values used in the European Union risk assessments). It is noted that the model is sensitive to the chosen OH concentration (NCM 2008).

Bahm and Khalil (2004) derived a 24 hour global annual average OH concentration of 9.2×10^5 molecules·cm^{-3}, with a value of 9.8×10^5 molecules·cm^{-3} for the northern hemisphere and 8.5×10^5 molecules·cm^{-3} for the southern hemisphere. These values are consistent with Prinn et al. (1995) and Montzka et al. (2000) who deduced OH concentrations from atmospheric measurements of methyl chloroform, reporting 24 hour global annual average values of $9.7(\pm0.6)\times10^5$ and $1.1(\pm0.2)\times10^6$ molecules·cm^{-3} respectively. Considering the uncertainty in the model estimates of kOH, the half-life for photochemical degradation of hexabromocyclododecane ranges from 0.4 to 4 days and 0.6 to 5.4 days for the northern and southern hemisphere respectively (EBFRIP 2009b).

(UNEP/POPS/POPRC.4/INF/13/Rev.1/Corr.1 section 2.2.3 of the POPRC Risk Profile).

4.1.4 Bioconcentration

From two flow-through bio-concentration tests with fish, A BCF of 18,100 in fathead minnow was chosen as a representative value in the EU risk assessment. hexabromocyclododecane levels have been shown to increase with trophic levels in a freshwater system: Fjeld (2008a) reported concentrations of hexabromocyclododecane in European smelt (*Osmerus eperlanus*), Vendace (*Coregonus albula*), and Brown Trout (*Salmo trutta trutta*) from lake Mjosa in Norway. European smelt and Vendace are important preyfish for the trout. The concentrations of hexabromocyclododecane detected in 2005 were 466 µg/kg lwt (8.8 µg /kg wwt), 374 µg /kg lwt (10.7 µg /kg wwt), 729 µg /kg lwt (18 µg /kg wwt) for the European smelt, the Vendace, and the Brown trout, respectively. HBCD has also been detected in other organisms high in rank in their food -chain such as birds, seals, marine fish, dolphins, harbour porpoise and polar bear.

(UNEP/POPS/POPRC.4/INF/13/Rev.1/Corr.1 section 2.2.3 of the POPRC Risk Profile; UNEP/POPS/POPRC.4/INF/13/Rev.1 section 3.2.3 of the Norwegian notification).

4.1.5 Persistence

Not or little degradation has been observed in water, soil and sediments. Furthermore, hexabromocyclododecane adsorbs to particles which slow down the degradation

Air: $T_{1/2}$ - 51.2 hours (Wania 2003, as referred in EC 2008)

Water: $T_{1/2}$ - 1140 hours (Wania 2003, as referred in EC 2008)

Soil: $T_{1/2}$ - 112-119 days (12°C) for γ-hexabromocyclododecane diastereomer

Aerobic sediment: $T_{1/2}$ – 197 days (recalculated to 12°C) for γ-hexabromocyclododecane in a simulation study.

(UNEP/POPS/POPRC.4/INF/13/Rev.1/Corr.1 section 2.2.3 of the POPRC Risk Profile; UNEP/POPS/POPRC.4/INF/13/Rev.1 section 3.2.3 of the Norwegian notification)

To evaluate the persistency of hexabromocyclododecane a compilation of data on experimentally measured half-lives in different environmental compartments, data on half-lives derived from modeling, and field data have been undertaken. Results of the estimation model, BIOWIN (v4.10, EPI Suite v4.0), which estimates the probability for aerobic biodegradation in the presence of mixed populations of environmental microorganisms suggest that hexabromocyclododecane is not readily biodegradable; the expected time of primary degradation is in the order of weeks. Moreover, an early biodegradation study using Closed Bottle Test systems (1) were conducted in accordance with OECD Guideline 301D, found no biodegradation of hexabromocyclododecane over a 28 day study period (Wildlife International 1996). It should be noted that while the studies were performed using accepted test guidelines, the concentrations tested were about three orders of magnitude greater (2) as the water solubility of hexabromocyclododecane (7.7 mg/L vs 66 µg/L).

Japanese authorities conducted a 28-day biodegradation study of 1,2,5,6,9,10-hexabromocyclododecane based on the OECD Test Guideline 301C. The degradation of the test substance, a mixture containing different stereoisomers, was assessed by high performance liquid chromatography. The percentage biodegradation of two hexabromocyclododecane isomeric forms (A and B1) were calculated to be 5 and 6%, respectively. (Chemicals Inspection and Testing Institute, 1990).

Several studies using sediment cores show that hexabromocyclododecane congeners deposited in marine sediments in Asia and in Europe at the beginning of the 1970s/1980s are still present in significant amounts (Minh et al. 2007, Tanabe 2008, Kohler et al. 2008, Bogdal et al. 2008), indicating a higher persistency in sediments than derived from experimental studies.

(UNEP/POPS/POPRC.4/INF/13/Rev.1/Corr.1 section 2.2.1 of the POPRC Risk Profile).

4.2 Effects on non-target organisms

4.2.1 Terrestrial vertebrates

A recent study with American kestrels indicates that a technical hexabromocyclododecane mixture administered to birds via the diet is readily taken

up and distributed to internal organs (BFR 2009a; SETAC 2009). The main stereoisomer detected in liver, fat and egg was α-hexabromocyclododecane, followed by γ-hexabromocyclododecane and β-hexabromocyclododecane. According to these observations, hexabromocyclododecane is preferentially stored in fat and is transferred to eggs during development. Tissue concentrations were such that fat>>eggs>liver>plasma (SETAC 2009). In this study, administration of 800 ng/g wwt of technical hexabromocyclododecane formulation in safflower oil for 21 days followed by a 25 day depuration period, resulted in environmentally relevant internal doses, i.e., sum of hexabromocyclododecane isomers of 934.8 ng/g lw (20 ng/g ww) in liver and 4216.2 ng/g lw (181. 5 ng/g ww) in eggs) with the level of α-hexabromocyclododecane being 164 ng/g wwt in egg) (BFR 2009b). A parallel study assessed reproductive effects of hexabromocyclododecane in American kestrels (*Falco sparverius*) (BFR 2009b; Dioxin 2010b). Also here kestrels were exposed daily to 800 ng/g wwt of a technical hexabromocyclododecane mixture in safflower oil from three weeks prior to pairing until two days before hatching. α-hexabromocyclododecane dominated in eggs, where it was found at a concentration of 164 ng/g wwt following exposure. While clutch size (number of eggs per female) was greater in the treated kestrels, hatchling numbers were comparable to that of controls (Dioxin 2010b). Treated kestrel nestlings were smaller in weight and had a slower growth rate than controls as determined by overall body weight. Behavioural parameters related to parental care were also affected by hexabromocyclododecane exposure (BFR 2009b; Dioxin 2010c).

(UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 2.4.3 of the POPRC Risk Profile).

4.2.2 Aquatic species

Ecotoxicity testing of hexabromocyclododecane in aqueous media is complicated by its very low water solubility and high adsorption potential (EBFRIP 2009b, NCM 2008), hexabromocyclododecane has a low acute toxicity to aquatic organisms owing in part to its limited solubility in aqueous media (Wildlife International 1997, Walsh et al. 1987, CEPA 2007 and ACCBFRIP 2001 for overview). Regarding the long-term toxicity of hexabromocyclododecane it was concluded to be very toxic to aquatic organisms in the EU Risk Assessment (European Union 2008). This conclusion was based on the long-term ecotoxicity test with *Daphnia magna* (28d-NOEC 3.1 µg/l; Wildlife International 1998) and on the growth inhibition test with *Skeletonema costatum* (72h-EC_{50} 52 µg/L; Wildlife International 2005). In both tests calculated NOEC and EC_{50} values were below the water solubility of the technical mixture of hexabromocyclododecane (66 µg/L). Based on the effects in long-term tests with *Lumbriculus variegates*, hexabromocyclododecane is known to cause adverse effects to aquatic sediment organisms at exposure level relevant for the environment (Institute of Hydrobiology 2001).

Fish-feeding studies indicate effects on key biological processes. For example an interference of hexabromocyclododecane with the HPT-axis and liver biotransformation enzymes were reported in rainbow trout exposed to individual hexabromocyclododecane diastereoisomers via food for 56 days followed by a depuration period of 112 days when fish were fed a reference diet (Palace et al. 2008). Lipid corrected concentrations of α-, β-, γ-isomers in the food were 29.14 ± 1.95, 11.84 ± 4.62, and 22.84 ± 2.26 ng/g, respectively (means ±SEM). Liver detoxification processes (P450 CYP1A activity) were inhibited by all hexabromocyclododecane stereoisomers after 7 days of dosing, and also after 56 days of dosing but then only in α- and β- exposed fish. Thyroid follicle epithelial cell heights were significantly greater in γ-hexabromocyclododecane exposed fish at day 56 of the uptake phase and in fish from the α- and γ-hexabromocyclododecane exposed groups at day 14 of the depuration phase. More recent studies also support that hexabromocyclododecane may interfere with the fish thyroid system (Palace et al. 2010). The link between hexabromocyclododecane induced disturbances in the HPT-axis and the importance of such effects to smoltification in Atlantic salmon has also been examined (Lower and Moore 2007). To assess this, Lower and Moore (2007) exposed juvenile salmon to 11 ng/L of a hexabromocyclododecane mixture for 30 days during the peak smoltification period in freshwater. The fish were then transferred to clean

seawater for 20 days. Throughout the hexabromocyclododecane-dosing and saltwater exposures, 5-8 fish were sampled every 7 days and gill and blood tissues were collected. In addition, electro-olfactrograms were recorded in an additional 5 fish every 10 days using urine from salmon from the same stream (considered to be the cue for returning smolts) as an effector. The exposure to hexabromocyclododecane was not observed to affect seawater adaptability, although the peak of thyroxine was shifted and occurred one week earlier in hexabromocyclododecane exposed fish than in controls. A reduction in olfactory function, as evidenced by attenuated olfactory responses during early freshwater transition, was also observed. This latter effect is important as it can affect successful homing, and thereby ultimately also reproductive capacity in adult salmon. In contrast to the above findings, in a third reported study assessing TH effects in European flounders (*Platichtys flesus*), no effects neither on the liver's biotransformation capacity or TH-levels were reported, even though hexabromocyclododecane accumulated dose-dependently (Kuiper et al. 2007). The fish were in this instance exposed to hexabromocyclododecane in food (µg/g lipid) and sediment (µg/g total organic carbon) in the following combinations; 0+0 (control); 0.3+0.08; 3+0.8; 30+8; 300+80; 3,000+800; and 0+8,000 for 78 days. Lastly, hexabromocyclododecane may also interfere with amphibian metamorphosis, a process that is tightly regulated by TH-hormones. As shown *in vitro*, hexabromocyclododecane at 10, 100 and 1000 nM potentiates T3 induced tadpole tail regression in a concentration dependent manner (Schriks et al. 2006). *In vivo* such effects may result in precocious metamorphosis.

Recent studies with fish models suggest that hexabromocyclododecane may also induce oxidative stress and apoptosis. Deng et al. (2009) examined oxidative stress and the apoptosis pathway in four-hour post-fertilization zebrafish (*Danio rerio*) embryos by exposing them to waterborne hexabromocyclododecane at concentrations of 0, 0.05, 0.1, 0.5, and 1.0 mg/ L for 92 hours. Survival was reduced at the three middle doses equivalently, but was elevated at the highest dose (1mg/L). Hatching rate was only affected at the highest dose (1 mg/L) with a 10% reduction from controls. Malformation rates (including epiboly deformities, yolk sac and pericardial edema, tail and heart malformations, spinal curvatures and improper inflation of the swimbladder) increased dose dependently, and heart rate and body length both also decreased with exposure to hexabromocyclododecane. The levels of reactive oxygen species (ROS) also increased dose dependently in fish exposed to hexabromocyclododecane concentrations above 0.05 mg/L. With regard to apoptosis, hexabromocyclododecane elevated expression of the pro-apoptotic genes p53, Bax, Puma, Apaf-1, and caspase-9 and caspase-3, of which the response of the latter two was verified at the enzyme level. The anti-apoptotic genes Mdm2 and Bcl-2 were both significantly down regulated at the highest hexabromocyclododecane exposure concentration. The overall results demonstrate that waterborne hexabromocyclododecane may produce oxidative stress in zebrafish embryos and lower survival at doses below the water solubility of technical hexabromocyclododecane. The latter effect is important since hexabromocyclododecane has been documented to be maternally transferred to offspring in oviparous animals, hereunder also fish (Nyholm et al. 2008, Jaspers et al. 2005, Lundsted-Enkel et al. 2006). The potential of hexabromocyclododecane to induce oxidative stress in zebra fish embryos has also been demonstrated by Hu et al. (2009). Here, the oxidative stress, assessed by lipid membrane damage (effects at 0.5, 2.5 and 10 mg /L) was also accompanied by delays in hatching (hexabromocyclododecane at ≤ 0.5 mg /ml), dose-independent changes in superoxide dismutase enzyme activity (higher at 0.1, lower at 2.5 and 10 mg/ L) and an elevation of heat shock proteins (Hsp70) activity (≥0.1 mg/L), the latter effect likely indicating increased protein repair activity. Moreover, in a study with Chinese rare minnows (*Gobiocyprinus rarus*) Zhang et al. (2008) observed a consistent increase in oxidative stress and cellular macromolecules in brain (ROS, carbonylation, TBARS) and erythrocytes (DNA) by waterborne hexabromocyclododecane in the 100-500 µg/l range (42 days). Protective enzymatic- (superoxide dismutase) and non-enzymatic antioxidant glutathione were compromised even at concentrations of 10 and 1 µg /L respectively. A shorter 28 day exposure resulted in somewhat higher effect concentrations. However, since

most test concentrations in these studies are above the water solubility of hexabromocyclododecane, the studies may not be suited to derive dose-response relationships and to set thresholds of toxicity.

In fish proposed novel mechanisms of hexabromocyclododecane toxicity are decreased protein metabolism and changes in cytoskeleton dynamics and cellular defense mechanisms (Kling and Förlin 2009). Recently, hexabromocyclododecane was also demonstrated to have a genotoxic potential and to increase cell death in benthic clams (*Macoma balthica*) (Smolarz and Berger 2009).

(UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 2.4.1 of the POPRC Risk Profile).

Hexabromocyclododecane is toxic to aquatic organisms such as *Daphnia magna*, a 21d-NOEC of 3.1 µg/l has been derived for a flow-through test.

Hexabromocyclododecane is not acute toxic to fish: In rainbow trout, no mortalities or other effects were observed in a 4-week toxicity test at a concentration of approximately 6.8 µg/l (mean measured concentration 2.5 µg/l).

(UNEP/FAO/RC/CRC.13/8 section 3.2.3 of the Norwegian notification)

Acute Aquatic Toxicity

Fish LC_{50}

Oncorhynchus mykiss 96-hour LC_{50} >0.0068 mg/L (nominal) or >0.0025 mg/L (mean measured)
(EPA, 2005; NICNAS, 2012; Reported in a secondary source. Guideline study. Performed according to current EPA, OECD guidelines and GLP. No toxicity at HBCD's limit of water solubility.)

Lepomis macrochirus 96-hour LC_{50} >100 mg/L (nominal)
(EPA, 2005; Reported in a secondary source with limited study details. Value exceeds water solubility.)

Leuciscus idus 96-hour LC_{50} >10,000 mg/L (nominal)
(EPA, 2005; Reported in a secondary source with limited study details. Value exceeds water solubility.)

Fish 96-hour LC_{50} = 0.30 mg/L (Estimated)
(ECOSAR v1.10; No effects at saturation (NES): The log K_{ow} of 5.6 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.)

Brachydanio rerio exposed to 0, 0.05, 0.1, 0.5 and 1.0 mg L for up to 96 hours.

- Cell apoptosis, induction of reactive oxygen species (ROS) at 0.1, 0.5 and 1.0 mg/L.
- Exposure to hexabromocyclododecane results in oxidative stress and may induce apoptosis throughinvolvement of caspases
- NOEC = 0.05 mg/L
- LOEC = 0.1 mg/L

(Deng et al., 2009; Guideline study. Study details taken from abstract. This study is for a nontraditional endpoint for determining hazard designation. In addition, NOEC and LOEC values are above the limit of water solubility and will not be

used to determine a hazard designation. No effects at saturation (NES) are predicted.)

Daphnid LC_{50} EC_{50}

Daphnia magna 48-hour EC_{50} >0.0068 mg/L (nominal) or >0.0032 mg/L (mean measured).

(EPA, 2005; NICNAS, 2012; Reported in a secondary source. Guideline study performed according to current EPA, OECD guidelines and GLP. No toxicity at HBCD's limit of water solubility; NES.)

D. magna 48-hour EC_{50} = 146 mg/L (nominal)

- Nominal test concentrations were 0.01-1,000 mg/L (both below and above the water solubility)

(EINECS, 2008; Reported in a secondary source. Guideline study performed according to current EPA, OECD guidelines and GLP. Value exceeds water solubility.)

Daphnia 48-hour LC_{50} = 0.23 mg/L (Estimated).

(ECOSAR v 1.10; NES: The log K_{ow} of 5.6 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.)

Green Algae EC_{50}

Skeletonema costatum 72-hour NOEC >0.01 mg/L (>10 µg hexabromocyclododecane)

- EC_{50} = 0.027 mg/L (biomass)
- EC_{50} = 0.052 mg/L (growth rate)

(Desjardins et al., 2005; ECHA, 2008; Reported in a secondary source with limited study details.)

Pseudokirchneriella subcapitata 96-hour EC_{50} >0.0068 mg/L (nominal) or >0.0037 mg/L (mean measured)

(EPA, 2005; NICNAS, 2012; Reported in a secondary source. Guideline study performed according to current EPA, OECD guidelines and GLP. No toxicity at HBCD's limit of water solubility; NES.)

Chlorella sp. 96-hour EC_{50} >1.5 mg/L

(EPA, 2005; NICNAS, 2012; Reported in a secondary source with limited study details. No toxicity at HBCD's limit of water solubility; NES.)

S. costatum 72-hour EC_{50} >0.0093-0.012 mg/L.

(EPA, 2005; NICNAS, 2012; Reported in a secondary source with limited study details. No toxicity at HBCD's limit of water solubility; NES.)

S. costatum 96-hour EC_{50} >0.0025 mg/L

(ECHA, 2008; Reported in a secondary source with limited study details. The test substance was made up of a composite of HBCD samples from three manufacturers containing 6.0% α-, 8.5% β- and 79.1% γ-diastereomers; total HBCD was 93.6% of test substance. There were no effects at the highest concentration tested.)

S. costatum 72-hour EC_{50} >0.0406 mg/L (40.6 µg/L)

- NOEC >0.0406 mg/L (only concentration tested)
- LOEC = Not identified

(Desjardins et al., 2004 (as cited in ECHA, 2008; NICNAS, 2012); Reported in a secondary source with limited study details; LOECs were not identified. One test concentration at the limit of water solubility; NES.)

Thalassiosira pseudonana 72-hour EC_{50} >0.05–0.37 mg/L

(Walsh et al., 1987 (as cited in EPA, 2005; NICNAS); Reported in a secondary source with limited study details. No toxicity at HBCD's limit of water solubility.)

Scenedesmus subspicatus 96-hour EC_{50} >500 mg/L

- No effect on growth inhibition

(Siebel-Sauer and Bias, 1987 (as cited in EINECS, 2008); Reported in a secondary source. Guideline study performed according to current EPA, OECD guidelines and GLP. Value exceeds water solubility.)

Green algae 96-hour EC_{50} = 0.29 mg/L (Estimated)

(ECOSAR v. 1.10; The estimated effect exceeds the water solubility of 0.66 mg/L, but not by 10x as required to be considered NES by ECOSAR.

Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.)

Chronic Aquatic Toxicity

Fish ChV

Oncorhynchus mykiss 88-day NOEC > 0.0037 mg/L (γ-hexabromocyclododecane).

27-Day hatching period:

- 61 days posthatch showed no effects on hatching success, time to swim-up, larval survival, fry survival or growth

(Drotter et al., 2001; EPA, 2005; Reported in a secondary source. Guideline study performed according to current EPA, OECD guidelines and GLP; LOEC and MATC could not be determined due to absence of toxicity, but were considered >0.0037 or 0.0068 mg/L (more than twice γ-HBCD's water solubility). HBCD was not chronically toxic to rainbow trout at concentrations at or above its limit of solubility.)

Fish ChV = 0.043 mg/L (Estimated)

(ECOSAR v. 1.10; Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.)

Chinese rare minnow 14-, 28- and 42-day waterborne hexabromocyclododecane exposure to 0.1-0.5 mg/L

- Induced hepatic enzymes (as measured by EROD and PROD).
- Induced oxidative stress in fish brain (as measured by ROS and TBARS).
- 28-day LOEC = 0.5 mg/L
- 42-day LOEC = 0.1 mg/L

(Zhang et al., 2008; Study details reported in abstract. Values exceed water solubility. This study is for a non-traditional endpoint for determining hazard designation. In addition, LOEC values are above the limit of water solubility and will not be used to determine a hazard designation. A NOEC was not identified.)

Daphnid ChV

D. magna 21-day life cycle toxicity test. Nominal test concentrations were 0.85, 1.7, 3.4 and 13.6 µg/L; measured test concentrations were 0.87, 1.6, 3.1, 5.6 and 11 µg/L.

- LOEC = 0.0056 mg/L ([0.0042 mg/L geometric mean]: reduced mean lengths)
- NOEC = 0.0031 mg/L (γ-hexabromocyclododecane, measured)

(Drotter and Kruger, 1998 (as cited in EINECS, 2008; EPA, 2005; NICNAS, 2012): Reported in a secondary source. Guideline study performed according to current EPA, OECD guidelines and GLP. Within the range of water solubility. The test substance was made up of a composite of HBCD samples from three manufacturers containing 6.0% α-, 8.5% β- and 79.1% γ-diastereomers; total HBCD was 93.6% of test substance. Reduced lengths, dry weight and fewer young observed in daphnia exposed to 0.011 mg/L.)

Daphnia ChV = 0.0.059 mg/L (Estimated)

(ECOSAR v. 1.10: Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.)

Green Algae ChV

Green algae ChV = 0.38 mg/L (Estimated)

(ECOSAR v. 1.10: The effect level exceeds the water solubility of 0.66 mg/L, but not by 10x as required to be considered NES by ECOSAR.

Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.)

Earthworm Subchronic Toxicity

Lumbriculus variegates 28-day sediment bioassay (spiked and aged sediment) with hexabromocyclododecane at 0.05, 0.5, 5, 50 and 500 mg /kg dwt (nominal)

- LOEC = 28.7 mg/kg (rate of emergence)
- NOEC = 3.2 mg/kg dwt
- Mean number of eggs in F1 generation was significantly reduced at highest concentration (159 mg/kg dwt).

(EINECS, 2008; Oetken et al., 2001; Performed in contrast with OECD Draft Guideline 218, artificial sediment with a coarse grain size (100-2,000 µm) and other carbon sources (stinging-nettle and leaves of alder). EINECS states that the results for total emergence and emergence rate were not considered valid for the purpose of risk assessment due to the large variations in solvent control.)

(UNEP/FAO/RC/CRC.13/INF/18 US EPA: Flame Retardant Alternatives for Hexabromocyclododecane (HBCD)).

4.2.3 Honeybees and other arthropods

Not available.

4.2.4 Earthworms

Long-term toxicity of hexabromocyclododecane to earthworms has been assessed by ABC (2003), who measured survival and reproduction in *Eisenia fetida* (clittelate adults) following 56 day exposure to a technical hexabromocyclododecane mixture. Hexabromocyclododecane was mixed dry into artificial soil media at concentrations of 78.5 to 5,000 mg/kg dry soil weight. In this study, the NOEC for survival and reproduction for hexabromocyclododecane were determined to be 4,190 and 128 mg/kg dry soil respectively. The NOEC for reproduction was later recalculated to 59 mg/kg dry soil weight because the soil that was used contained a higher amount of organic matter than standard soil (NCM 2008).

		(UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 2.4.2 of the POPRC Risk Profile).
4.2.5	**Soil microorganisms**	For effects of hexabromocyclododecane on soil micro-organisms, the only conducted study reports a NOEC of ≥ 750 mg /kg dw using nitrate production as an endpoint for assessment (ECT 2007). (UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 2.4.2 of the POPRC Risk Profile).
4.2.6	**Terrestrial plants**	Not available.
5	**Environmental Exposure/Risk Evaluation**	
5.1	**Terrestrial vertebrates**	Collectively, the findings from studies suggest that there is reason for concern of reproductive and developmental effects in wild birds, because the 800 ng/g wwt dose that elicited effects in the studies by Marteinson and Fernie (see BFR 2009 for overview) are similar to what have previously been observed in wild birds in Central Europe and the Norwegian Arctic, i.e., (cormorant (liver): 138-1.320 ng/g lw and tern (egg): 330-7100 ng/g lw (Morris et al. 2004); glaucous gulls (liver):195-15.027 ng/g lw and great black- backed gulls (liver): 1.881 - 3.699 ng/g lw (KLIF 2007); glaucous gulls (liver): 75.6 ng/g wwt (Verreault et al. 2007). (UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 2.4.3 of the POPRC Risk Profile). Further indications for concern come from recent preliminary data obtained with captive American kestrels which suggest a risk for reproductive and developmental effects in source regions. The findings from Marteinson et al. (Dioxin 200910c) and Fernie et al. (Dioxin 2010cb) suggest that there is reason for concern of reproductive and developmental effects in wild birds, not only because of the seasonal changes in fat stores experienced by wild birds and the observed transfer to eggs, but also because the 800 ng/g wwt dose and the subsequent *in ovo* hexabromocyclododecane concentrations that elicited effects in these studies are similar to what has previously been observed in wild birds in Central Europe, i.e., cormorant liver, 138-1.320 ng/g lw; and, tern eggs, 330-7100 ng/g lw (Morris et al. 2004). In the study, administration of 800 ng/g wwt of technical hexabromocyclododecane formulation in safflower oil for 21 days followed by a 25 day depuration period, resulted in environmentally relevant internal doses, i.e., the sum of hexabromocyclododecane isomers, 934.8 ng/g lw (20 ng/g ww) in liver; and, 4216.2 ng/g lw (181. 5 ng/g ww) in eggs (with the level of α-hexabromocyclododecane being 164 ng/g wwt in eggs) (BFR 2009b; SETAC 2009). Endocrine disruptor effects may arise from low dose exposure and are highly dependent on the timing of exposure (WHO and IPCS, 2002). The study on American kestrels (BFR 2009b; Dioxin 2010c) also suggests a risk for reproductive and developmental effects in wild birds in remote regions, where the internal doses (164 ng/g wwt of α-hexabromocyclododecane) that elicited effects in the studies by Marteinson and Fernie (BFR 2009b) is exceeded by internal doses observed in wild birds in the Norwegian Arctic, i.e. glaucous gulls (liver), 195-15.027 ng/g lw; and, great black- backed gulls (liver), 1.881 - 3.699 ng/g lw (KLIF 2007); glaucous gulls (liver): 75.6 ng/g wwt (Verreault et al. 2007). Muir et al. (2004) detected hexabromocyclododecane isomers in concentrations in the blubber of beluga whales (*Delphinapterus leucas*) in the Canadian Arctic in 2001, a species protected by the Convention on migratory species. The concentrations were in the range of 9.8-18 ng/g lw. Muir et al. (2006) detected levels of hexabromocyclododecane in adipose tissue of polar bears (*Ursus maritimus*) in several populations in the Arctic region in 2002. The highest levels were detected in the female bears from the Svalbard area (109 ng/g lw). Effects on polar bears and other marine mammals were not investigated in these studies. (UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 2.4.6 of the POPRC Risk Profile).
5.2	**Aquatic species**	A comparison of measured concentrations in the tissues and organs of species of prey (fish) with the predicted no-effect concentration (PNEC) for secondary poisoning for hexabromocyclododecane reveals that the concentrations in fish exceed the PNEC of 5 mg/kg food for predators (mammals and birds) both near

local point-sources and source regions. In the vicinity of point sources such as the river Skerne in the UK and the river Scheldt basin in Belgium, hexabromocyclododecane concentrations above 5 mg/kg wwt have been measured in fish (eel and brown trout). Also in marine mammals, concentrations higher than the PNEC have been measured, the highest being 6.4 mg/kg wwt whole body weight in harbour porpoise from the UK (European Union 2008). The potential risk of hexabromocyclododecane to wild life near local point-sources and source regions is further supported by the body/tissue residue based risk assessment made by EBFRIP (2009b). Notably the upper third of the monitoring data used in the assessment exceeds the specific-toxicity residue-based PNEC for freshwater fish and for mammals. The upper limit of the monitoring data for birds also enters this range.

Hexabromocyclododecane has been detected in many Arctic species (invertebrates, birds, fish, terrestrial and marine mammals). Levels in Polar cod from Svalbard (Arctic Norway) have been reported at 1.38-2.87 ng/g lipid weight (see levels and effects tables in UNEP/POPS/POPRC.6/INF/25). The findings of hexabromocyclododecane in fish in remote regions suggest a potential for endocrine effects considering the laboratory studies done by Lower and More (2007), Palace et al. (2008 and 2010) showing effect on the thyroid axis for salmoid fish.

(UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 2.4.6 of the POPRC Risk Profile).

5.3 Honey bees

Not available.

5.4 Earthworms

Not available.

5.5 Soil microorganisms

Not available.

5.6 Summary – overall risk evaluation

Hexabromocyclododecane is persistent in the environment and has a strong potential to bioaccumulate and biomagnify in food chains.
α-hexabromocyclododecane appears to be the more persistent of the isomers of hexabromocyclododecane and to biomagnify more than β-hexabromocyclododecane and γ-hexabromocyclododecane.
Hexabromocyclododecane is widespread in the global environment and biota; elevated levels are found in top predators and other threatened species in the Arctic. Releases of hexabromocyclododecane to the environment are increasing in all regions investigated. The increasing standing masses of construction materials are potentially long-term sources of hexabromocyclododecane to the environment, as well as representing larger releases when demolished or renovated in the future. Releases during recycling of construction materials and electronic appliances can be of importance and are likely to increase in the future. A general trend seems to be that α-hexabromocyclododecane dominates in the upper trophic levels while the main isomer in the lower levels appears to be γ-hexabromocyclododecane. In human tissue α-hexabromocyclododecane seems to predominate in the general population. Most toxicological studies with hexabromocyclododecane focus on hexabromocyclododecane mixtures and the available data on stereoisomer specific toxicity is very limited.

Hexabromocyclododecane is considered very toxic to aquatic organisms. There is a risk of adverse effects in marine mammals and fish in the vicinity of point sources and in regions with elevated background levels. The measured concentration levels in biota exceed the PNEC for secondary effects of 5 mg/kg wwt in the EU risk assessment of hexabromocyclododecane (European Union 2008). Levels in birds from European regions with elevated back ground levels or near local point sources are concluded to lie near the threshold levels for adverse effects. In avian species, preliminary data from recent studies report effects such as reduced eggshell thickness, growth and survival. Further indications for concern come from recent preliminary data obtained with captive American kestrels which suggest a risk for reproductive and developmental effects also in wild birds in remote regions.

Both older and recent available literature suggest that hexabromocyclododecane can induce effects in mammals and that both chronic and subchronic, high and low

dose exposure to hexabromocyclododecane may have wide ranging and potentially severe effects, particularly to the neuroendocrine system and to offspring during early phases of development. Hexabromocyclododecane has a potential to interfere with the hypothalamic-pituitary-thyroid (HPT) axis and cause reproductive and developmental effects. Many effects were trans-generational and affected both parents and offspring. Hexabromocyclododecane is maternally transferred to offspring, both in humans and in wildlife.

In addition to the findings in the *in vivo* animal studies, there are a large number of recent *in vitro* studies that document how hexabromocyclododecane upon adsorption may act on, and possibly interfere with biological processes such as cell homeostasis, protein repair, metabolism, intracellular signalling and neuroendocrine processes. Such studies add to the understanding that exposure to hexabromocyclododecane has various effects on human health and the environment, and should also be regarded when considering the toxicity of hexabromocyclododecane.

(UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 3 of the POPRC Risk Profile)

Annex 2 – Details on final regulatory actions reported

Country Name: Japan

1	**Effective date(s) of entry into force of actions**	1 May 2014
	Reference to the regulatory document	The Chemical Substances Control Law (CSCL) and its Enforcement Order.
2	**Succinct details of the final regulatory action(s)**	This chemical is designated as a Class I Specified Chemical Substance. It is prohibited to manufacture, import or use this chemical substance.
3	**Reasons for action**	The regulatory action was based on concerns related to human health.
4	**Basis for inclusion into Annex III**	The regulatory action was taken to protect human health. The regulatory action was based on a risk evaluation taking into account the prevailing conditions in Japan.
4.1	**Risk evaluation**	This chemical is persistent, highly bioaccumulative and has long-term toxicity to humans. (UNEP/FAO/RC/CRC.13/8 Section 2.4.2.1 of the Japanese notification)
		When a substance is listed to the Stockholm Convention, and when it is on the market in Japan, the Japanese Government conducts a risk evaluation on the substance and its potential risks to inform the regulatory measures. This internal risk evaluation, in combination with the Risk Profile document for hexabromocyclododecane, were supplied as supporting information by Japan in document UNEP/FAO/RC/CRC.13/INF/17/Rev.2. A brief English summary of that domestic risk evaluation was provided along with the table of contents of the risk evaluation.
		The internal risk evaluation was based on the monitoring data from fiscal year 2009 to fiscal year 2012 and revealed a number of sites with a high ecological risk, while there were no sites with any human health risk. The risk evaluation included a hazard assessment, an exposure assessment and risk estimation based on monitoring data, and an exposure assessment and risk estimation based on environmental releases estimated from manufacture data.
		The notification from Japan indicates that the regulatory action was based on a risk or hazard evaluation and specifically cites the Risk Profile document for hexabromocyclododecane as prepared by the POPRC (UNEP/FAO/RC/CRC.13/8 section 2.4.1 of the Japanese notification). The POPRC document cites a Japanese study (Kakimoto et al. 2008) which found hexabromocyclododecane levels in human milk appear to mirror the market consumption of hexabromocyclododecane. In mothers' milk from Japanese women (age 25–29) hexabromocyclododecane levels were below the detection limit in all samples collected during the 10-year period from 1973-1983, but then increased from 1988 onwards. In the period 1988-2006, α-hexabromocyclododecane was detected in all 11 pooled milk samples with levels ranging from 0.4-1.9 ng/g lw. Mean total hexabromocyclododecane concentrations over the period 2000 – 2006 ranged from 1-4 ng/g lw. (UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 2.3.2 of the Risk Profile document)
		The Risk Profile document states the developmental- and neurotoxic potential of hexabromocyclododecane observed in animal studies give cause for concern when considering risks to human health, particularly for unborn babies and young children (UNEP/FAO/RC/CRC.13/INF/17/REV.2 section 2.4.6 of the Risk Profile document).
4.2	**Criteria used**	Risk to human health.
	Relevance to other States and Region	The notifying Party did not provide information on the relevance to other States and Regions.
5	**Alternatives**	The notifying Party did not provide information on alternatives to

		hexabromocyclododecane.
6	**Waste management**	The notifying Party did not provide information on waste management of hexabromocyclododecane or articles containing it.
7	**Other**	None.

Country Name: Norway

1	**Effective date(s) of entry into force of actions**	9 July 2016
	Reference to the regulatory document	Hexabromocyclododecane is regulated by Chapter 4 of the Regulation related to restrictions on the manufacture, import and placing on the market of chemicals and other products hazardous to human health and the environment (Product Regulation) act no. 922 of June 2004. This is the Norwegian implementation of Regulation (EC) No 850/2004 of the European Parliament and of the Council on persistent organic pollutants and the implementation of the amendment to its Annex I. Commission Regulation (EU) 2016/293 of 1 March 2016.
2	**Succinct details of the final regulatory action(s)**	Regulations to restrict production, import, export and sale of consumer products that contain hexabromocyclododecane exceeding certain limit values.
3	**Reasons for action**	The regulatory action was based on concerns related to human health and the environment.
4	**Basis for inclusion into Annex III**	The final regulatory action was taken to protect human health and the environment. The regulatory action was based on a risk evaluation taking into account the prevailing conditions in Norway.
4.1	**Risk evaluation**	The notification from Norway indicates that the regulatory action was based on a risk or hazard evaluation and that it was relevant to both human health and the Environment. The notification specifically cites the European Union Risk assessment for hexabromocyclododecane (UNEP/FAO/RC/CRC.13/8 section 2.4 of the Norwegian notification). Summarized in the body of the notification from Norway is evidence of exposure to consumers in Norway, its detection in the environment (including remote areas of the arctic), biota, fish, moss, yolk sac of newly hatched chicks. Some temporal trends are noted such as the increase in hexabromocyclododecane levels in eggs from Atlantic puffins and Atlantic cod liver. The abstracts of the scientific articles presented in the supporting information from Norway (UNEP/FAO/RC/CRC.13/INF/18) confirm the occurrence of hexabromocyclododecane in the environment and biota in Norway and its surroundings, and some cases of increasing concentrations over time. Hazard endpoints identified in the United States Environmental Protection Agency 2014 report, *Flame Retardant Alternatives for Hexabromocyclododecane (HBCD)* are also provided in the supporting information from Norway. High or very high hazards are noted for developmental effects, acute aquatic toxicity, and chronic aquatic toxicity. Hexabromocyclododecane is highly persistent and has very high bioaccumulation. (UNEP/FAO/RC/CRC.13/INF/18)
4.2	**Criteria used**	Risk to human health and the environment.
	Relevance to other States and Region	The Stockholm Convention has agreed on listing hexabromocyclododecane in Annex A (ban), with exemptions for production and use in expanded polystyrene and extruded polystyrene in buildings. The global ban was introduced 26 of November 2014.
5	**Alternatives**	The notifying Party provided the US EPA document: United States Environmental Protection Agency: Flame Retardant Alternatives for Hexabromocyclododecane (HBCD). Final report June 2014.
6	**Waste management**	The notifying Party did not provide information on waste management of hexabromocyclododecane or articles containing it.
7	**Other**	None.

Annex 3 – Addresses of designated national authorities

Japan	
CP	
From PIC Website (20 November 2017): Name: Mr. Kentaro Mizuuchi Job title: Deputy Director Department: Global Environment Division / International Cooperation Bureau Institution: Ministry of Foreign Affairs Postal address: 2-2-1 Kasumigaseki, Chiyoda-ku 100-8919 Tokyo Japan	Phone: +81 3 5501 8245 Fax: +81 3 5501 8244 Email: kentaro.mizuuchi *a* mofa.go.jp

Norway	
C	
From PIC Website (20 November 2017): Name: Ms. Christel Moræus Olsen Job title: Senior Advisor, Rotterdam Convention Designated National Authority for Industrial Chemicals and Biocides Institution: Norwegian Environment Agency Postal address: Grensesvingen 7 0661 Oslo Norway	Phone: +47 735 80 500 Fax: +47 735 80 501 Email: christel.moraeus.olsen *a* miljodir.no; pic *a* miljodir.no

C Industrial chemicals
CP Pesticides and industrial chemicals

Annex 4 – References

Regulatory actions

Japan
The Chemical Substances Control Law (CSCL) and its Enforcement Order.

Norway
Hexabromocyclododecane is regulated by Chapter 4 of the Regulation related to restrictions on the manufacture, import and placing on the market of chemicals and other products hazardous to human health and the environment (Product Regulation) act no. 922 of June 2004. This is the Norwegian implementation of Regulation (EC) No 850/2004 of the European Parliament and of the Council on persistent organic pollutants and the implementation of the amendment to its Annex I, Commission Regulation (EU) 2016/293 of 1 March 2016.

Supporting documentation provided by Japan

- POPRC (2010). Risk profile on hexabromocyclododecane. UNEP/POPS/POPRC.6/13/Add.2
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